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A SYSTEMATIC REVIEW OF SYSTEMATIC REVIEWS FOR EFFECTIVENESS OF INTERNAL FIXATION FOR FLAIL CHEST AND RIB FRACTURES IN ADULTS

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ABSTRACT

Objectives

Multiple systematic reviews have reported on the impact of rib fracture fixation in the presence of flail chest and multiple rib fractures however, this practice remains

controversial. Our aim is to synthesise the effectiveness of surgical fixation of flail chest and ribs fractures as evidenced by systematic reviews.

Design

A systematic search identified systematic reviews comparing effectiveness of rib fracture fixation with non-operative management of adults in the presence of flail chest or multiple rib fractures. Risk of bias was assessed using the ROBIS tool.

Results

Twelve systematic reviews were synthesised. Length of mechanical ventilation was shorter in the fixation group compared to the non–operative group in flail chest; pooled estimates ranged from -4.52 days, 95% CI [-5.54, -3.5] to -7.5 days, 95% CI [-9.9,-5.5]. Pneumonia, length of hospital and ICU stay all showed a statistically significant improvement in favour of fixation; however all outcomes in favour of fixation had substantial heterogeneity. Mortality rate did not statistically improve with fixation compared to non-operative management. Two systematic reviews reported multiple rib fracture fixation but due to lack of evidence were not able to confer any benefit of fixation over non-operative management.

Conclusions

The synthesis has shown some statistically significant improvement in patient outcomes with flail chest after internal surgical fixation. However due to differences in indications and timing of fixation in the primary studies, results are confounded by substantial clinical heterogeneity. For future review updates, meta-analysis for effectiveness may need to take into account indications and timing of surgery as a subgroup analysis to address clinical heterogeneity between primary studies.

Study Registration

PROSPERO ID 42016053494

KEY WORDS

Rib fracture; Flail chest; Multiple rib fractures; Internal fixation; Systematic review; meta-analysis; mortality; mechanical ventilation; length of hospital stay; pneumonia

STRENGTHS AND LIMITATIONS OF THIS STUDY

- Multiple databases were searched for studies and study selection was undertaken by two researchers, reducing the risk of error
- Risk of bias of studies was assessed using the ROBIS tool by two researchers
- Primary research within the reviews was assessed to identify if the reviews were based on the same primary evidence
- Synthesises all identified reviews regardless of risk of bias

INTRODUCTION

Severe chest wall injuries which include multiple rib fractures (adjacent unifocal fractures) and flail chest (three or more adjacent bifocal rib fractures with paradoxical chest wall movement) have high morbidity and mortality (18.7%) due to the associated complications of acute respiratory distress syndrome, pneumonia and haemorrhage.[1] Chest trauma present in 15% of all trauma admissions[2] with the most common mechanism of injury, a road traffic accident (57.01%) and falls accounting for the second biggest proportion(22.96%).[1] Flail chest in particular has a high mortality rate as chest wall biomechanics are disrupted causing an increase in the work of breathing for patients who are often in significant pain.

Current treatment options for multiple rib fractures and flail chest are generally supportive measures including oral and regional anaesthesia, and non-invasive and invasive ventilation.[3] Surgical fixation is thought to be beneficial to patients with respiratory failure,[4] intractable pain[5] or if failing to wean from invasive ventilation secondary to flail chest or multiple rib fractures.[6 7] Surgical fixation has the potential to restore chest wall biomechanics and reduce the respiratory complications associated with poor ventilation and secretion clearance.[7] Due to the rapidly, albeit heterogeneous, growing evidence base from multiple systematic reviews it is essential to synthesise evidence for this intervention to ascertain safety and efficacy.

This report is part of a wider systematic review to (i) identify and synthesise the evidence of the effectiveness of internal surgical rib fracture fixation, (ii) to evaluate the evidence for indications and timing of surgical fixation, and (iii) to identify the outcomes reported in the literature. Systematic reviews and primary studies were eligible for inclusion. This paper maps and synthesises the systematic review evidence assessing the effectiveness of internal surgical fixation of rib fractures.

METHODS

The review was undertaken systematically using the methods described by the Centre for Reviews and Dissemination.[8] The protocol was registered on PROSPERO and can be accessed at https://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42016053494.

Eligibility criteria

Population

The eligible population were adults (over 18 years) who have sustained one or more rib fractures following blunt chest trauma, with or without pulmonary contusion. Single rib fracture, multiple rib fractures and flail chest injuries were included but treated as separate injuries and therefore reported and analysed separately. Patients with penetrating injuries were excluded. Studies of mixed populations with penetrating and non-penetrating injuries were included only if data were presented separately for the two groups. Surgery for chronic non-union was excluded.

Intervention

Any method of internal surgical fixation such as plate or strut fixation; metal or synthetic material including intramedullary splints and suture fixation were eligible for inclusion.

Comparator

External surgical fixation (defined as traction methods, splints and Hoffman style pin and bar fixation) and non-surgical management (such as supportive ventilation, epidural and regional anaesthesia).

Outcomes

All outcomes were eligible for inclusion (e.g. mortality, pain and pneumonia). The primary outcome of interest was duration of mechanical ventilation due to the close relationship with mortality and morbidity of ventilator associated complications.

Study design:

Inclusion: Systematic reviews were included if they specified a search strategy in at least one literature database and included primary research. No restrictions were placed on the study design of the primary studies.

Exclusion: Literature reviews that did not have a defined research question, search strategy or defined process of selecting articles.

Search strategy

An electronic database search was undertaken on 14 December 2016 and updated on 13 March 2017. Searches for systematic reviews included the following databases: MEDLINE including PreMEDLINE, EMBASE, Cochrane Database of Systematic Reviews (CDSR) and Science Citation Index. Clinical guidance, policy documents and relevant databases such as NICE Evidence were searched. These included the UK Department of Health policy content, National Clinical Guideline Centre, and Scottish Intercollegiate Guidelines Network (SIGN). An additional search for non-published literature within the Conference Proceedings Citation Index was undertaken.

The start date for the MEDLINE searches was 1976 as that was the year that Advance Trauma Life Support was introduced internationally, incorporating new methods of resuscitation which have significantly improved outcomes. No other restrictions were applied.

The search strategy, developed for MEDLINE, is provided in **Supplementary File 1** and was adapted to run appropriately on other databases. To identify relevant further reviews reference lists of included studies were assessed for eligibility.

Selection

Searches were downloaded into Endnote X7 (Clarivate Analytics, Version 7.1 release date 2/04/2014) and de-duplicated. Two researchers (HI and EC) independently screened titles and abstracts. Any paper classified as potentially eligible by either reviewer was ordered as a full text and independently screened by both reviewers. It was originally planned to have second screening of only 50% but resources allowed for full duplicate

screening. A third researcher reviewed disagreements (CM) where a consensus could not be reached between the researchers.

Data extraction

Extracted data included patient characteristics; intervention and comparators, outcome measures, as well as duration of follow up, and effect estimates, standard errors and confidence intervals as available. Outcomes that were not subject to meta-analysis and were presented as a narrative synthesis in the systematic reviews were extracted and presented as a narrative synthesis and included effect sizes, standard deviations and significance values. A description of study methods and information about the study including country and year were also extracted.

One researcher completed data extraction (HI); a second researcher cross-checked 50% (EC). Discrepancies were cross-checked by both researchers at a second review and a consensus reached.

Risk of bias

Quality assessment with the ROBIS Tool[9] was undertaken by one researcher(HI) and checked by a second (CM). Discrepancies were resolved by discussion.

Data synthesis

All types of internal surgical fixation were synthesised as one group. Flail chest and multiple rib fractures are considered different injuries and have been synthesised separately for each outcome extracted. Each outcome was narratively synthesised including number of reviews using the outcome and effect estimates with 95% confidence intervals from the source review. Important numerical data was presented in tables for all outcomes measured. All outcomes that were reported in the reviews were included in the report to avoid reporting bias.[10] Although not fully applicable, reporting was in accordance as much as possible with the PRISMA statement.[11]

Protocol Deviations

The registered protocol encompasses a larger body of work which includes synthesis of primary research for effectiveness, indications for surgery, timing of surgery and mapping of outcome measures. Only the synthesis of systematic reviews is reported here. Although all outcomes were extracted and presented in tables only those that were measured in two or more studies were narratively synthesised.

Patient involvement

Patients were not involved in the preparation or conduct of this review.

RESULTS

Electronic searches identified 791 records; an additional 39 records were collected following reference checking. The full text screening identified 12 systematic reviews eligible for inclusion, there were 21 papers excluded because they were not classified as systematic reviews. The PRISMA flow diagram in **Error! Reference source not found.** shows the screened records and reasons for exclusions. **Supplementary File 2** lists the excluded studies.

Review characteristics

Eleven systematic reviews and one rapid evidence synthesis, published by NICE as an overview for the Interventional Procedures Advisory Committee (IPAC)[12], published between 2010 and June 2016 met the inclusion criteria. Table 1 provides a summary of review characteristics. Three of the reviews are presented as best evidence topics [13] by Schulte et al.[14] Girsowicz et al.[15] and de Lesquen et al.[16]

Table 1 Review characteristics

Review Year Country	Review aim	Search strategy	Studies and participants	PICOS	Risk of bias	Authors' Conclusions
Swart [17] **2016** **USA**	To perform a meta-analysis of high quality literature to evaluate both economic and medical benefits of early fixation of rib fractures in severe chest trauma	PubMed, Embase, Medline and Scopus, No search start date Last search date 1 June 2016 Search terms defined, No limitations described Evidence of hand searching Eligibility criteria - over 18 years of age and studies comparing operative vs non-operative treatment	3 RCT n =123 14 Case Control 3 Case Series	**Population** Acute flail chest 18 years or old **Intervention** Operative Fixation **Comparator** Non-operative **Studies Type** All study designs	No evidence of quality assessment	Acute ORIF of rib fractures in patients with flail chest injuries results in reduced mortality and medical complications in conjunction with being cost effective intervention.
Schuurmans [18] **2016** **Netherlands**	Investigate how operative management improves patient care for adults with flail chest.	PubMed, Trip database, Google Scholar No search start date Last search date November 2015 Search terms defined, No limitations described Evidence of reference checking Eligibility criteria - studies comparing operative vs non-operative treatment, RCT only and English	3 RCT n = 123	**Population** Acute flail chest **Intervention** Operative Fixation **Comparator** Non-operative **Studies Type** RCTs	Quality assessment completed but criteria and explanation unclear	The operative management group showed a significant lower incidence of pneumonia, whereas mortality rate did not differ between treatment groups.
Schulte [14] **2016** **UK**	In patients with acute flail chest does surgical rib fixation improve outcomes in terms of morbidity and mortality?	OVID MEDLINE® Search start date 1946 Last search date January 2016 Search terms defined Search strategy description minimal, No limitations described No evidence of reference checking No specific inclusion or exclusion criteria defined.	1 Meta-analysis by separate author 1 RCT n=123 (2 further coded as RCT which are non-randomised studies) 3 Retrospective cohort studies	**Population** Acute flail chest **Intervention** Operative Fixation **Comparator** Non-operative **Studies Type** Unclear	No evidence of quality assessment	Surgical stabilization of flail chest in thoracic trauma patients has beneficial effects with respect to reduced ventilatory support, shorter intensive care and hospital stay, reduced incidence of pneumonia and septicaemia, decreased risk of chest deformity and an overall reduced mortality when compared with patients who received non-operative

						management.
Coughlin [19] **2016 UK**	Compare the efficacy of flail chest surgical stabilisation to non-operative management	PubMed MEDLINE, Embase, Cochrane Library, clinical trials.gov. No search start date Last search date February 2015 Search terms defined, No limitations Evidence of reference checking Eligibility criteria - studies comparing operative vs non-operative treatment in flail chest and RCT only	3 RCT n = 123	**Population** Traumatic flail chest **Intervention** Surgical stabilisation of any kind **Comparator** Patients treated non-operatively by any other means **Studies Type** RCTs only	Clear quality appraisal of the studies	Surgical stabilisation for a traumatic flail chest is associated with significant clinical benefits including rate of pneumonia, length of hospital an ICU stay and duration of mechanical ventilation in this meta-analysis of three relatively small RCTs
Unsworth [20] **2015 Australia**	To review the treatments for blunt chest trauma and their impact on patient and hospital outcomes. Specifically alludes to surgical stabilization of flail chest.	Cochrane, Medline, EMBASE and CINAHL databases Search limited to 1990 onwards Last search date March 2014 Search terms defined. Limited to humans and adults Evidence of reference checking Eligibility criteria - original research, blunt chest trauma, intervention for blunt chest trauma including a comparator and contained measured outcomes	3 RCT n =123 5 Retrospective Case Controls n= 642 1 Retrospective cohort n = 21	**Population** Adult blunt chest trauma Flail chest **Intervention** Multidisciplinary Intervention (Models of care, management intervention, care practices, care protocols) **Comparator** Other intervention not specified **Studies Type** RCTs	Some quality assessment completed but criteria and explanation unclear	Across the literature there were consistent improvements in patients with flail chest and surgical fixation with fewer days of mechanical ventilation, ICU-LOS and cost savings compared to non-operative techniques. Three out of nine studies were randomized controlled trials, and the level of evidence in all studies was primarily fair or good.
De Lesquen [16] **2015 France**	In flail chest is open reduction and internal fixation needed?	Medline and Science Direct Search start date limited to 1994 onwards Last search date January 2014 Search Terms defined	2 Meta-analysis 3 RCT n = 123 1 prospective cohort n = 60	**Population** Blunt chest trauma. Flail chest **Intervention**	No evidence of quality assessment	For flail chest, early surgical stabilization can be considered in patients who would require mechanical ventilation for >48 h

		No evidence of hand searching or reference checking Eligibility criteria - Exclusions of both child and vascular injuries	5 Retrospective cohort n = 238	Open reduction and internal fixation **Comparator** Unclear **Studies Type** Unclear		
Cataneo [21] 2015 Brazil	To evaluate the effectiveness and safety of surgical stabilization compared with clinical management for people with flail chest	Cochrane Injuries Group Specialised Register, CENTRAL, Medline, Embase, CINAHL, SCI, CPCI-S, Clinical trials.gov, ICTR No search start date Last search Date 12th May 2014. Search terms defined, No limitations Evidence of reference checking Eligibility criteria - RCTs.	3 RCTs n = 123	**Population** Adults or children with flail chest **Intervention** Surgical stabilisation of any kind **Comparator** Clinical management included any type of chest wall stabilization without surgical intervention such as straps or bags and any type of ventilatory assistance. **Studies Type** RCTs only	Clear quality appraisal of the studies	There was no evidence that surgical intervention reduced mortality in people with FC compared with nonsurgical management. There was some evidence that surgical intervention could reduce the risk of developing pneumonia and thoracic deformity; need for tracheostomy; duration of mechanical ventilation, length of ICU stay, and hospital stay; and chronic pain, but the trials to date have been small. There is an urgent need for larger high-quality randomized con-trolled trials.
De Jong [22] 2014 Netherlands	To specify indications for rib fracture fixation of non-flail chests	Medline, Cochrane, Embase Search start date limited to 2010 Last search date December 2013 Search terms defined, limited to year 2000 onwards. Evidence of reference checking Eligibilty criteria - Studies included at least 10 participants who were surgically treated for non-flail chest rib fractures. Reported in English, Dutch, or German. Excluded were case reports, biomechanical studies, animal studies, and expert opinions.	1 Case Control n = 60 2 Cohort studies n = 47	**Population** Traumatic non-flail chest **Intervention** Surgical treatment of non-flail chest **Comparator** Unclear **Studies Type** All studies with at least 10 surgically treated	No evidence of quality assessment	The evidence for surgical treatment of non-flail chest rib fractures is limited

Slobogean [23] **2013 Canada**	Compare the critical care outcomes of surgical fixation to non-operative management in patients with flail chest injuries	Medline, Embase, Cochrane Database of Systematic Reviews (CDSR), and the Cochrane Central, Register of Controlled Trials (CENTRAL) No search start date Last search date May 2011 No limitations No evidence of reference checking or hand searching Eligibility criteria - Comparator studies with more than 10 cases.	2 RCT 1 case control n= 60 8 Cohort n = 676	**Population** Acute flail chest **Intervention** Operative Fixation **Comparator** Conservative management **Studies Type** RCTs	No evidence of quality assessment	Improved outcomes of multiple critical care outcomes with narrow confidence intervals but based on small retrospective studies. Suggests prospective RCT to overcome potential biases
Leinicke [24] **2013 USA**	Comparing operative to non-operative therapy in adult flail chest patients	MEDLINE (1966-2012), Embase (1947-2012), Scopus (all years), Cochrane Databases and ClinicalTrials.gov Last search date February 2012 Search terms defined, limited to English and human studies Evidence of reference checking Eligibility criteria - studies comparing operative vs non-operative treatment in patients with flail chest. Excluded case reports and case series	2 RCT 3 Case Control n=158 4 Cohort n = 303	**Population** Flail chest **Intervention** Operative Fixation **Comparator** Non-Operative **Studies Type** RCTs, cohort, and case-control trials	Clear quality appraisal of the studies	As compared to non-operative therapy, operative fixation of FC is associated with reductions in DMV, LOS, mortality, and complications associated with prolonged MV. These findings support the need for an adequately powered clinical study to further define the role of this intervention
Girsowicz [15] **2012 France**	In patients over 45 years old with isolated, movable and painful rib fractures without true flail chest is surgical stabilization superior to non-operative management in improving outcomes?	OVID Medline 1948 –2011 Last search date June 2011 Search terms defined, limited to Human and English language Evidence of reference checking Eligibility criteria – excluded flail chest but inclusions not well described	4 Retrospective cohort n= 107 1 non-systematic Review 1 Case control = 30 2 Case report n= 2	**Population** Over 45 years old with isolated, movable and painful Rib fractures without true flail chest **Intervention** surgical stabilization **Comparator** non-operative management **Studies Type** Unclear	Some comments on strengths and weaknesses but no quality or risk of bias assessment	Surgical stabilization in the management of isolated multiple non-flail and painful rib fractures improved outcomes (pain, respiratory function, quality of life and reduced socio-professional disability) Studies provided a low level of evidence (small studies with few numbers of patients and short-term follow-up or case reports). Large prospective controlled trials are thus necessary to confirm these encouraging results.

NICE Evidence [12] **2010** **UK**	To make recommendations about the safety and efficacy of surgical rib fracture fixation in flail chest	MEDLINE, PREMEDLINE, EMBASE, Cochrane Library No search start date Last search date May 2010 Search terms defined No limitations No evidence of reference checking but other searches performed Eligibility criteria – clinical studies of patients with flail chest operated with metal rib reinforcements and published in English. Excluded conference abstracts and reviews	1 RCT 2 non randomized studies 4 case series Total 225 patients	**Population** Flail chest **Intervention** Insertion of metal rib reinforcements. **Comparator** Unclear **Studies Type** Clinical studies were included. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded	No evidence of quality assessments	Surgical rib fracture fixation should be consider in patients with flail chest
RCT = Randomised controlled trial, ORIF = Open reduction internal fixation, ICU = Intensive care unit, LOS = Length of stay, FC = Flail chest, MV = Mechanical ventilation, DMV = duration of mechanical ventilation						

Nine reviews[12 14 16-19 21 23 24] evaluated the effectiveness of internal surgical fixation in patients with flail chest, two reviews included patients with multiple rib fractures[15 22] and one review included all rib fractures but only reported outcomes for flail chest.[20] Although single rib fractures were included in the protocol none of the primary studies assess fixation of a single rib fracture. The inclusion criteria specified only adult patients in ten reviews, with Girsowicz et al.[15] specifically looked at patients over the age of 45 years old. Although studies of children were eligible in the review by Cataneo et al.[21], none of the primary studies in the review included any participants less than 18 years of age. Studies specified all types of surgical fixation and did not specifically exclude external fixation however, no primary study had external fixation in their intervention or comparator groups.

Three reviews[18 19 21] included only randomised evidence and eight included other study designs[12 14-17 22-24] (two systematic reviews, 19 non-randomised studies, 11 case series and two case reports) (Table 2). As would be expected, there was overlap across the review in the included primary studies The total number of patients who had internal fixation in primary studies (excluding duplicate studies) was 1036 and there were 1187 controls.

Table 2 Primary studies included in each review and the number of included patients

Review	Leinicke et al. (2013)	Slobogean et al. (2013)	Tanaka (2001)	Granetzny (2005)	Marasco (2013)	Paris (1975)	Kim (1981)	Karev (1997)	Ahmed et al. (1995)	Voggenreiter (1998)	Balci et al. (2004)	Teng (2009)	Nirula et al (2006)	Althausen et al. (2011)	De Moya (2011)	Granhed et al. (2014)	Doben et al. (2014)	Jayle et al. (2015)	Pieracci et al. (2015)	Zhang et al. (2015)	Wada et al. (2015)	Xu et al. (2015)	Majercik (2015)	Defreest (2016)	Ohresser (1972)	Hellberg (1981)	Menard (1983)	Moulton (1997)	Cacchione et al., (2000)	Lardonois (2001)	Kerr -Valentic (2003)	Gasparri et al., (2003)	Borrelly (2005)	Campbell (2009)	Mayberry (2009)	Richardson et al., (2007)	Moreno De La (2010)
Intervention patients			18	20	23	18	18	40	26	20	27	32	30	22	16	60	10	10	35	24	84	17	38	41	14	10	18	23	1	66	40	1	127	32	46	7	22
Control Patients			19	20	23	11	45	93	38	22	37	28	30	28	32	153	11	10	35	15	420	15	57	45	-	-	-	-	-	-	-	-	-	-	-	-	-
Swart [17]			●	●	●		●	●	●	●	●	●	●	●	●	●	●	●		●	●	●	●	●													
Schuurmans [18]			●	●	●																																
Schulte [14]		●												●	●	●	●	●	●	●	●	●															
Coughlin [19]			●	●	●																																
Unsworth [20]			●	●	●				●	●			●	●	●		●																				
de Lesquen [16]	●	●	●	●	●			●	●	●	●		●	●																							
Cataneo [21]																																					
de Jong [22]													●																					●	●		
Slobogean [23]			●	●			●	●	●	●	●	●	●												●								●				
Leinicke [24]			●	●				●		●	●		●	●	●																						
Girsowicz [15]													●																●		●	●		●	●	●	●
NICE [12]			●			●				●																●	●	●		●							
	SR		RCT			Non Randomised Study																			Case Series or Report												

The rapid evidence synthesis by NICE[12] was the first review published in 2010. It included seven primary studies including one RCT published in 2001.[25] Another trial[26] published in 2005 was not included in the review despite it appearing to meet the inclusion criteria. Search terms may have missed this study as it was not reported in the excluded studies list. A review in 2015 by Cataneo et al.[21] was the first meta-analysis published and included three RCTs.[25-27] Two further systematic reviews published since then[18 19] have identified the same three RCTs and repeated the same meta-analyses. The research question and eligibility criteria in both of the reviews are almost identical to the review by Cataneo et al.[21] and they were both published in 2016. The best evidence topic review by Schulte et al.[14] included the most recent RCT[27] however, it was unclear why the two earlier RCTs[25 26] were not included as there were no study date restrictions, and there was no excluded studies list to check this.

Risk of bias

The ROBIS tool identified seven studies were rated as low risk of bias,[12 16 18 19 21 23 24] three as unclear[15 17 22] and two as high.[14 20] The two reviews rated as having high risk of bias were due to lack of detail in the search strategy, no attempts to minimise errors of data extraction by double checking and no quality assessment of included studies.

The only review for which a protocol was identified was the Cochrane review undertaken by Cataneo et al.[21] A search of PROSPERO identified no registered protocols for any of the other included reviews, Table 3 contains a summary of the risk of bias assessment for each review.

Table 3 Risk of bias using ROBIS tool

Studies	Study eligibility criteria	Identification and selection of studies	Data collection and study appraisal	Synthesis and findings	Risk of bias in the review
Swart 2016 [17]	Low	Unclear	High	High	Unclear
Schuurmans 2016[18]	Low	Unclear	High	Low	Low
Schulte, 2016 [14]	High	High	High	High	High
Coughlin 2016 [19]	Low	Low	Low	Low	Low
Unsworth 2015 [20]	Low	Low	Unclear	Unclear	High
de Lesquen, 2015 [16]	Unclear	High	Unclear	Unclear	Low
Cataneo, 2015 [21]	Low	Low	Low	Low	Low
de Jong, 2014 [22]	High	Unclear	High	High	Unclear
Slobogean, 2013 [23]	Low	Low	High	Low	Low
Leinicke, 2013 [24]	Low	Low	Low	Low	Low
Girsowicz, 2012 [15]	High	High	High	High	Unclear
NICE Evidence, 2010 [12]	Low	Unclear	Unclear	Low	Low

Outcome evaluation

All reviews undertook a narrative synthesis with six reviews including a meta-analysis.[17-19 21 23 24] Table 4 summarises the results of the meta-analysis by outcome for flail chest. Table 5 details the results from the systematic reviews for flail chest which undertook a narrative synthesis and Table 6 for narrative synthesis related to multiple rib fractures. Across all the reviews eighteen outcomes were reported. Eleven outcomes were reported by more than one review, seven further outcomes were reported by only a single review.

Primary outcome - Length of mechanical ventilation (days)

Flail Chest

Ten systematic reviews reported length of mechanical ventilation; six of these reported a meta-analysis[17-19 21 23 24] with four[17-19 21] reporting a meta-analysis on the same three RCTs.[25-27]

There was substantial variation across the reviews in the pooled estimates for this outcome, related to pooling different sets of studies. The largest reduction in duration of mechanical ventilation with surgical fixation compared to non-operative management was reported by Slobogean et al.[23] who pooled two RCTs[25 26] and six non-randomised studies [28-33] (MD (fixed) -7.5 days, 95% CI [-9.9,-5.5]); (Table 4). The mean difference was 3 days

more than the pooled estimates by Leinicke et al.[24] and Swart et al.[17]. Leinicke et al. [24] pooled six non-randomised studies[5 28 29 31 33 34] and two RCTs[25 26] and reported a statistically significant reduction of -4.52 days, 95% CI [-5.54, -3.50];Swart et al.[17] pooled three RCTs[25-27] and 15 non-randomised studies[5 28 29 31-42] and reported a statistically significant reduction of -4.57 days, SD (0.59).

Table 4 Results of individual reviews that report a meta-analysis for flail chest

Studies reporting outcome	N of studies (n of participants in analysis)	Study Types		Details of meta-analysis	Results	I^2
		RCT	NR			
Total length of invasive mechanical ventilation (Days)						
Cataneo [21]	3 (123)	3	0	MD [IV, Fixed, 95% CI]	Results not pooled	-
Coughlin [19]	3 (123)	3	0	MD [IV, Random, 95% CI]	-6.30 [-12.16, -0.43]	95
Leinicke [24]	8 (474)	2	6	MD [IV, Random 95% CI]	−4.52 [−5.54, −3.50]	48.6
Schuurmans [18]	3 (123)	3	0	MD [IV, Random, 95% CI]	−6.53 [−11.88, −1.18]	93
Slobogean [23]	8 Studies (563)	2	6	MD [IV, Fixed, 95% CI]	-7.5 [-9.9, -5.0]	48
Swart [17]	18 Studies (1150)	3	15	MD [IV, Random, SD]	-4.57 [0.59]	83
Mortality (frequency)						
Cataneo [21]	3 (123)	3	0	RR [M-H, Fixed, 95% CI]	0.56 [0.13, 2.42]	0
Coughlin [19]	2 (86)	2	0	RR [M-H Random 95% CI]	0.57 [0.13, 2.52]	0
Leinicke [24]	5 (343)	1	0	RR [95% CI]	0.43 [0.28, 0.69]	0
Schuurmans [18]	2 (86)	2	0	RR [M-H, Fixed, 95% CI]	0.56 [0.13, 2.42]	0
Slobogean [23]	7 (582)	2	5	OR [M-H, Fixed, 95% CI]	0.31 [0.20, 0.48]	-
Slobogean [23]	7 (582)	2	5	RR [M-H, Fixed, 95% CI]	0.19 [0.13, 0.26]	0
Swart [17]	13(1263)	3	10	RR [M-H, Random, SD]	0.44 [0.09]	0
Total length of stay in intensive care unit (Days)						
Cataneo [21]	2 (77)	2	0	MD [IV, Fixed, 95% CI]	Results not pooled	-
Coughlin [19]	3 (123)	3	0	MD [IV, Random, 95% CI]	-6.46 [-9.73, -3.19]	35
Leinicke [24]	5 (235)	2	3	MD [IV, Random, 95% CI]	−3.4 [−6.01, −0.80]	74.9
Schuurmans [18]	3 (123)	3	0	MD [IV, Fixed, 95% CI]	−5.18 [−6.17, −4.19]	40
Slobogean [23]	4 (261)	2	2	MD [IV, Fixed, 95% CI]	-4.8 [-7.9, -1.6]	0.1
Swart [17]	14 (840)	3	11	MD [IV, Random, SD]	-3.25 [1.29]	91
Total length of stay in hospital (Days)						
Coughlin [19]	2 (86)	2	0	MD [IV, Random, 95% CI]	-11.39 [-12.39, -10.38]	0
Leinicke [24]	5 (262)	1	4	MD [IV, Random 95% CI]	−3.83 [−7.12, −0.54]	68.9
Schuurmans [18]	2 (86)	2	0	MD [IV, Fixed, 95% CI]	−11.39 [-12.39,−10.38]	0
Slobogean [23]	4 (404)	1	3	MD [IV, Fixed, 95% CI]	-4.0 [-7.4, -0.7]	33
Swart [17]	11(438)	1	10	MD [IV, Random, SD]	-4.48 [1.98]	89

Pneumonia (frequency)						
Cataneo [21]	3 (123)	3	0	RR [M-H Random 95% CI]	0.36 [0.15, 0.85]	66
Coughlin [19]	3 (123)	3	0	RR [M-H Random 95% CI]	0.36 [0.15, 0.85]	66
Leinicke [24]	4 (260)	1	3	RR [95% CI]	0.43 [0.28, 0.69]	31
Schuurmans [18]	2 (83)	2	0	RR [M-H, Fixed, 95% CI]	0.45 [0.29, 0.7]	74
Slobogean [23]	8 (816)	2	6	OR [M-H, Fixed, 95% CI]	0.18 [0.11, 0.32]	4
Slobogean [23]	8 (816)	2	6	RR [M-H, Fixed, 95% CI]	0.31 [0.21, 0.41]	4
Swart [17]	15 (1005)	3	12	RR [M-H, Random, SD]	0.59 [0.10]	55
Tracheostomy (frequency)						
Cataneo [21]	2 (83)	2	0	RR [M-H Random 95% CI]	0.38 [0.14, 1.02]	64
Leinicke [24]	4 (215)	1	3	RR [95% CI]	0.25 [0.13, 0.47]	0
Schuurmans [18]	2 (83)	2	0	RR [M-H, Fixed, 95% CI]	0.4 [0.2, 0.7]	Not reported
Slobogean [23]	3 (165)	1	2	OR [M-H, Fixed, 95% CI]	0.12 [0.04, 0.32]	0
Slobogean [23]	3 (165)	1	2	RR [M-H, Fixed, 95% CI]	0.34 [0.10, 0.57]	0
Swart [17]	11 (975)	2	9	RR [M-H, Random, SD]	0.52 [0.07]	42
Sepsis (frequency)						
Slobogean [23]	4 (345)	0	4	OR [M-H, Fixed, 95% CI]	0.36 [0.19, 0.71]	0
Slobogean [23]	4 (345)	0	4	RR [M-H, Fixed, 95% CI]	0.14 [0.56, 0.23]	0
Spirometry (percentage of predicated)						
Coughlin [19]	-	-	-	-	-	-
FVC	2 (74)	2	0	MD [IV, Random, 95% CI] p-value	1.53 [-13.49, 16.55] p = 0.84	Not reported
FEV1	2 (74)	2	0	MD [IV, Random, 95% CI] p-value	-0.42 [-4.83, 3.98] p = 0.85	Not reported
TLC	2 (74)	2	0	MD [IV, Random, 95% CI] p-value	3.69 [-3.08, 10.46] p = 0.29	Not reported
PEFR	2 (74)	2	0	MD [IV, Random, 95% CI] p-value	0.38 [-0.76, 1.53] p = 0.51	Not reported
Chest deformity (frequency)						
Cataneo [21]	2 (86)	2	0	RR [M-H, Fixed, 95% CI]	0.13 [0.03, 0.67]	0
Slobogean [23]	4 (228)	1	3	OR [M-H, Fixed, 95% CI]	0.11 [0.02, 0.60]	2.1
Slobogean [23]	4 (228)	1	3	RR [M-H, Fixed, 95% CI]	0.30 [0.00,0.60]	2.1
Dyspnoea (frequency)						
Slobogean [23]	3 (135)	1	2	OR [M-H, Fixed, 95% CI]	0.40 [0.16, 1.01]	0

Slobogean [23]	3 (135)	1	2	RR [M-H, Fixed, 95% CI]	0.15 [0.09, 0.39]	0
Chest pain (frequency)						
Slobogean [23] Slobogean [23]	2(71) 2(71)	1 1	1 1	OR [M-H, Fixed, 95% CI] RR [M-H, Fixed, 95% CI]	0.40 [0.01, 12.60] 0.18 [0.46, 0.83]	0 0
RCT= Randomised controlled trial, NR = Non randomised study, RR = Risk ratio, OR = Odds ratio, MD = Mean difference, SD = Standard deviation, CI = Confidence interval, IV - Inverse variance, M-H - Mantel-Haenszel, FVC = Force vital capacity, FEV1 = Forced expiratory volume, TLC = Total lung capacity, PEFR = Peak expiratory flow rate						

There were differences in the data reported for the four meta-analyses of mechanical ventilation[17-19 21] that included the same three RCTs. Schuurmans et al.[18] extracted median duration of mechanical ventilation post randomisation from the Marasco et al. RCT[27] (operative, median 9 days (SD 3.8) Vs. non-operative, median 10.8 days (SD 5.9)) and pooled this in the meta-analysis along with studies that measured mean total time on ventilation. In contrast, Coughlin et al.[19], Cataneo et al.[21] and Swart et al.[17] report the total mean time on mechanical ventilation, which they state, was obtained directly from the authors (operative, mean 6.32 (SD 3.46) Vs. non operative, mean 7.54 (SD 5.42)). The pooled estimates using the median and mean data from the Marasco RCT[27] are broadly similar and show a reduction in mechanical ventilation of more than 6 days, though the difference is slightly larger in the Schuurman et al.[18] review (MD -6.53 days, 95% CI [-11.88, -1.18]) than the Cataneo et al.[21], Coughlin et al.[19] and Swart et al.[17] reviews (MD -6.30 days, 95% CI [-12.16, -0.43]).

Variations also arose in relation to the extraction of data from the RCT by Granetzny et al.[26] who did not publish standard deviations for the outcome length of mechanical ventilation within their publication. Slightly different SD values are found in all six meta-analyses[17-19 21 23 24] which may have arisen from different methods of imputation and all give slightly different estimates.

Substantial heterogeneity was seen in all meta-analyses reporting this outcome[18 19 23 24] (I^2 = 48% to 95%). Cataneo et al.[21] did not pool the data from the three RCTs included for this outcome due to the substantial statistical heterogeneity (I^2= 95%) but reported the individual study effect estimates from all three RCTs. A statistical difference is reported in two RCTs[25 26] (-7.50 days, 95% CI [-11.18, -3.82] and -10.00 days, 95% CI [-10.37, -9.63]) and a non-statistical difference in the other RCT[27] (-1.21 days 95% CI [-3.84, 1.42]) in favour of surgical fixation compared to non-operative management.

Narrative synthesis from two reviews concluded that fixation reduces the length of mechanical ventilation compared to non-operative management.[16 20] (Table 5)

Table 5 Results of individual reviews that report a narrative synthesis for flail chest

Study details	Included studies	Outcomes assessed	Narrative Synthesis
Author Unsworth [20] **Year** 2015 **Country** Australia	RCT = 2 Granetzny(40) Tanaka (37) Marasco (46) Non randomised= 6 Ahmed (64) Althausen (50) Doben (21) De Moya (48) Nirula(60) Voggenreiter (42) Total number of patients = 408	• Mortality • Pneumonia • Pneumothorax and haemothorax • Hospital length of stay • ICU stay • Costings • Treatment outcome	• Significant decrease in mechanical ventilation requirements after surgical fixation. decreasing in ventilator-acquired pneumonia after surgical fixation • decrease in ICU-LOS, fewer days of mechanical ventilation and cost savings compared to non-operative management • decreased days of ventilator dependence, and shorter ICU-LOS • lower incidence of pneumonia, a higher return to full time work at six months • less persistent pain at six and 12 months in those receiving surgery • significantly fewer days of mechanical ventilation and a shorter hospital and ICU-LOS • The estimated cost savings ranged from US Dollars 10,000 to AU Dollars 14,443 per patient with surgical rib fixation as a result of the decrease in ICU-LOS. • None of the studies were large enough to draw conclusions on the effect of this intervention on thromboembolism and death.
Author de Lesquen [16] **Year** 2015 **Country** France	Meta-analysis = 2 Leneike 9 studies (538 patients) Slobogean 11 studies (732 patients) RCT = 3 Marasco (46) Granetzny(40) Tanaka (37) Non-randomised= 6 Ahmed (64) Karev (40) Voggenreiter (20) Balci (64) Nirula(60) Althausen(50) Total number of patients=421	• Duration of IMV • LOS ICU • Pneumonia • Mortality	For flail chest, early surgical stabilization can be considered in patients who would require mechanical ventilation for >48 h (Grade B, extrapolated recommendations from Level I evidences).

Author NICE [12] **Year** 2010 **Country** UK	RCT = 1 Tanaka (37) Non-randomised = 2 Voggenreiter (42) Paris (29) Case Series = 4 Lardinois (66) Mouton (23) Menard (18) Hellberg (10) Total number of patients=225 Intervention group = 173 Control group = 52	• Duration of IMV • Mortality • LOS ICU • Pneumonia • Lung function • Return to Employment • Sepsis • Pain or discomfort requiring removal of plates	Surgical stabilisation with metal rib reinforcements aims to allow earlier weaning from mechanical ventilation, reduce acute complications and avoid chronic pain sometimes associated with permanent malformation of the chest wall. Kirschner wire may be used on its own, but this method of ribstabilisation is not covered by this guidance.
Author Schulte [14] **Year** 2016 **Country** UK	Systematic Review = 1 Slobogean (753) RCT = 1 Marasco (23,23) Non-randomised studies = 9 Jayle (10,10) Pieracci (35,35) Zhang (24,15) Wada (84,336) Granhed (60,153) Doben (10,11) Xu (17,15) Althausen (22,28) De Moya (16,32) Total number of patients=1712 Intervention group = 301 Control group = 658	• Duration of IMV • Mortality • LOS hospital • LOS ICU • Pneumonia	Surgical stabilization of flail chest in thoracic trauma patients has beneficial effects with respect to reduced ventilatory support, shorter intensive care and hospital stay, reduced incidence of pneumonia and septicaemia, decreased risk of chest deformity and an overall reduced mortality when compared with patients who received non-operative management.
ICU = Intensive care unit, IMV = invasive mechanical ventilation, LOS = Length of stay, RCT = Randomised controlled trial			

Multiple rib fractures

Two systematic reviews[15 22] included one primary study[31] that reported length of mechanical ventilation for multiple rib fracture patients (Table 6). The cohort study which had matched non-operative controls[31] reported a statistically significant reduction in post-operative ventilator days ($p = 0.02$) in favour of the fixation group; however there was no statistical difference in total ventilator days ($p = 0.12$). It was unclear what the non-operative treatment consisted of.

Table 6 Results of individual reviews that report a narrative synthesis for multiple rib fractures

Study details	Included studies	Outcomes assessed	Narrative Synthesis
Author de Jong [22] **Year** 2014 **Country** Netherlands	RCT = 0 Non-randomised = 1 Nirula (60) Case Series = 2 Campbell (32) Mayberry (46, 15 non-flail) Total number of patients=138 Intervention group = 108 Control group = 30	• LOS hospital • Duration of IMV • Time of operation • Chronic pain	Only Nirula et al. concluded that rib fracture fixation showed a trend toward fewer total ventilator days. Mayberry et al. investigated the quality of life after rib fixation, and they concluded that there was low long-term morbidity and pain. Campbell et al. demonstrated low levels of pain and satisfactory rehabilitation.
Author Girsowicz [15] **Year** 2012 **Country** France	Non-systematic review =1 Nirula and Mayberry Case Comparator = 1 Nirula (30,30) Case Series = 4 Mayberry (46) Richardson (7) Barajas (22) Campbell (32) Case report = 3 Gasparri (1) Cacchione (1) Kerr-Valentic (1) Total number of patients=169 Intervention group = 139 Control group = 30	• Pain • Disability • Respiratory function • Number of days lost from work	In general, of the nine studies presented, all indicated that surgical stabilization in the management of isolated multiple non-flail and painful rib fractures improved outcomes. Indeed, the interest and benefit was shown not only in terms of pain and respiratory function but also in improved quality of life and reduced socio-professional disability. Hence, the current evidence shows surgical stabilization to be safe and effective in alleviating post-operative pain and improving patient recovery, thus enhancing the outcome of the procedure. However, retrieved studies provided a low level of evidence (small studies with few numbers of patients and short-term follow-up or case reports). Large prospective controlled trials are thus necessary to confirm these encouraging results.
IMV = invasive mechanical ventilation, RCT = Randomised controlled trial			

Mortality

Flail Chest

Seven systematic reviews reported mortality; six of these pooled the data in a meta-analysis[17-19 21 23 24] and one reported data as a narrative synthesis[16]. Three systematic reviews[18 19 21] which pooled the same three RCTs[25-27] showed a non-statistically significant reduction in mortality with internal surgical fixation compared to non–operative management (RR (Fixed) 0.56, 95% CI [0.13, 2.42][18 21] and RR (Random) 0.57, 95% CI [0.13, 2.52][19] (Table 4)).

Three systematic reviews pooled randomised and non-randomised studies.[17 23 24] The most recent review,[17] pooled the three RCTs[25-27] and ten non randomised studies.[5 28-43] This review demonstrated there was a statistically significant reduction in mortality with surgical fixation compared to non-operative treatment (RR (random) 0.44, SD (0.09)[17]). The later reviews[23 24] were published before the RCT by Marasco et al.[27] and hence were not included in the meta-analyses (RR (fixed) 0.43, 95% CI [0.28, 0.69] and RR (fixed) 0.19, 95% CI [0.13, 0.26], respectively). Overall, statistical heterogeneity was low (I^2=0%) for this outcome in all studies that presented this data.[17-19 21 23 24]

Multiple rib fractures

Mortality was not assessed in the reviews by de Jong et al.[22] or Girsowicz et al.[15]

Length of ICU Stay (days)

Flail Chest

Eight systematic reviews[12 16-19 21 23 24] assessed length of ICU stay; six of these performed a meta-analysis.[17-19 21 23 24] Pooled estimates ranged from -3.25 days [SD 1.29][17] to -6.46 days, CI 95% [-9.73, -3.19][19] and were all in favour of surgical fixation compared to a variety of comparators (Table 4). The range in pooled estimates may be partly explained by the pooling of different sets of studies.

Three reviews included the same RCT[27] but the data extracted from the RCT for this outcome varied across reviews. Differences occurred as some pooled median length of ICU stay and others pooled the mean. Furthermore, some used postoperative time spent in ICU and others the total time spent in ICU.[17-19]

Variation also arose across reviews in the data extracted from another trial due to standard deviations not being reported in the primary publication.[26] Imputation values were calculated or the raw data obtained from the authors resulting in SD values ranging from 0.7 to 4.4 and 2.2 to 7.3 in the operative and non-operative groups respectively. There was also a substantial difference in the effect estimate of this study[26] in one of the reviews[24] compared to the data included in the other reviews. The data reported in this review was -10 days, 95% CI [-15.41, -4.59] which is 5 days greater than the data from the same study included in other reviews. It is the same as the as length of mechanical ventilation effect estimate reported in the same study[26] so is possibly a transcription error.

Statistical heterogeneity ranged from substantial to none[44] for this outcome with I^2 values of 74.9%[24], 40%[18], 35%[19] and 0.1%[23]. The narrative syntheses concluded that in patients with flail chest undergoing surgical fixation length of ICU stay was reduced compared to non-operative management.[16 20]

Multiple rib fractures

A single review reported length of stay in ICU for patients with multiple rib fractures[15]. Within this review one non-randomised study reported a reduction in ICU days but this was not statistically significant (p =0.51), however the mean difference and 95% CIs were not reported [31].

Length of Hospital Stay (days)

Flail Chest

Nine systematic reviews[12 16-21 23 24] assessed length of hospital stay and six of these reported a meta-analysis.[17-19 21 23 24] Two of the systematic reviews[17 21] pooled the same two trials[25 26]

for length of stay in hospital and found a significantly shorter hospital length of stay in favour of the operative group compared to non-operative management (MD -11.39 days 95% CI [-12.39, -10.38]). When non-randomised studies were included in the meta-analysis the pooled effects were smaller (-3.83 days, 95% CI [-7.12,-0.54],[24] -4 days, 95% CI [-7.4, -0.7][23] and -4.48 days, SD (1.98)[17] in favour of fixation; Table 4).

When pooling the two RCTs in the systematic reviews, heterogeneity was low $I^2 = 0$,[18 19], however when pooling a greater number of studies including non – randomised studies the heterogeneity was moderate to substantial, ($I^2 = 89\%$,[17] $I^2 = 68.9\%$[24] and $I^2 = 33\%$[23] respectively).

In the narrative synthesis by one review,[20] they reported that in patients with flail chest undergoing surgical fixation the length of hospital stay was less in one non-randomised study[34] and in one RCT[26] in the fixation group compared to the non-operative group. No data or significance values were reported in this review.

Multiple rib fractures

Two systematic reviews[15 22] included a single non-randomised study that assessed length of hospital stay (days).[31] This study reported a shorter total hospital stay in the operative group (mean 18.8 days (SD 1.8)) compared to the non-operative group (mean 21.1 days (SD 3.9) (p=0.59)).

Pneumonia

Flail Chest

Ten systematic reviews[12 16-19 21 23 24 45], assessed pneumonia and six of these reported a meta-analysis for this outcome.[14 17-21 23 24] In all of the reviews, the risk of developing pneumonia was found to be lower in the surgical fixation group compared to the non-operative group. Three RCTs[25-27] were pooled in two of the reviews[16 17] and they found a risk reduction of 0.36, 95% CI [0.15, 0.85], in favour of operative fixation compared to non-operative management. When non-randomised studies were combined the risk reductions

ranged from 0.31, 95% CI [0.21, 0.41] to 0.45, 95% CI [0.29, 0.70] in favour of fixation (Table 4).

Substantial heterogeneity was seen in meta-analyses for this outcome[18 19 21] that included the three RCTs[25-27] (I^2 = 66% to 74%). In the reviews that pooled the RCTs alongside the non-randomised studies[23 24] there were lower levels of heterogeneity (I^2 = 4% and I^2 = 31%, respectively).

Two narrative syntheses reported that among patients with flail chest undergoing surgical fixation the risk of pneumonia were reduced in the fixation group compared to the non-operative group.[16 20] One review[20] included two non-randomised studies[34 35] and two RCTs[25 26] but the conclusions could not be verified as there were no effect estimates, confidence intervals or significance values reported. The other review,[16] included four non-randomised studies[29 33-35] and three RCTs,[25-27] four of the included studies report a statistically significant reduction [25 29 33 34] ($p<0.05$) and three a non-statistically significant reduction in pneumonia associated with the intervention.[26 27 35]

Tracheostomy

Flail Chest

Five systematic reviews included a meta-analysis of the outcome of tracheostomy.[17 18 21 23 24] Pooled relative risks within each review ranged from 0.25, 95% CI [0.13, 0.47] to 0.40, 95% CI [0.2, 0.7] (Table 4).

Moderate and substantial heterogeneity was seen in two reviews (I^2=42%[17], I^2=64% [21]), two reviews [23 24] had low heterogeneity (I^2=0%), and one did not report heterogeneity [18].

Sepsis

Flail Chest

One review,[23] pooling four non-randomised studies[30 33 35 46] estimated a RR of 0.14, 95% CI [0.56, 0.23] with I^2=0% in favour of fixation compared to non-operative management. The estimate RR reported is not possible given the confidence interval does not include the

estimated value, 0.14. The lower interval of 0.56 could possibly be -0.56 creating a wider CI and would suggest that the author's conclusion was correct and there was a statistically significant difference in favour of fixation. The odds ratio is also presented for the same pooled analysis and reported as 0.36, 95% CI [0.19, 0.71], I^2=0%.

Spirometry

Flail Chest

One of the reviews[19] reported a meta-analysis of spirometry data which included two RCTs[26] [27] with spirometry measured at two different time points (three and two months respectively). No statistically significant differences in any spirometry data were seen between surgical fixation and non-surgical approaches (Table 4).

Chest Deformity

Flail Chest

Two reviews reported a meta-analysis of chest deformity.[23] [21] Both reported a statistically significant effect estimate in favour of surgical fixation compared to non-operative management (RR 0.30, 95% CI [0.00, 0.60], I^2=2.1% and RR 0.13, 95% CI [0.03 to 0.67], I^2=0%).

Dyspnoea

Flail chest

One review[23] pooled studies reporting dyspnoea in a meta-analysis and included one RCT[25] and two non-randomised studied.[35] [47] They reported a difference in favour of surgical fixation with a pooled risk ratio of 0.15, 95% CI [0.09 to 0.39]; however, when these data were expressed as odds ratios the results were no longer statistically significant (OR 0.40, 95% CI [0.16, 1.01]). Duration of follow-up for this outcome was one year for two of the primary studies[47] [25] and unclear in the third.[35] It was unclear how dyspnoea was measured or defined in the three primary studies.

Chest Pain

Flail chest

Chest pain was reported in one systematic review[23] which included two primary studies (one RCT[25] and one non-randomised study[47]) and data were pooled in a meta-analysis which suggested a benefit in favour of fixation (OR 0.40, 95% CI [0.01, 12.60] and RR 0.18, CI 95% [0.46, 0.83]).

Other reported outcomes

Several other outcomes were reported within the systematic reviews however no others have been pooled in a meta-analysis. A narrative synthesis was not completed on the outcomes: wound infection, pain-requiring removal of metalwork, return to work, socio-professional disability cost, pulmonary embolism, pneumothorax and haemothorax. In the reviews, data on these additional outcomes was minimal and presented as a narrative synthesis without presenting numerical data (Table 5 and Table 6).

DISCUSSION

Twelve systematic reviews were identified that focused on the effectiveness of surgical fixation for flail chest and multiple rib fractures and were reported between 2010 and 2016. This is the first systematic review of reviews and highlighted that there are a large number of reviews focusing on the same aims and including the same primary studies.

Flail chest

Six[17-19 21 23 24] of the 12 systematic reviews presented meta-analyses for flail chest based on overlapping primary studies. They reported reductions in length of mechanical ventilation, length of stay, pneumonia and tracheostomy rates with surgical fixation compared to non-operative management and inconsistent results for mortality. Across many of the meta-analyses there was moderate to high levels of heterogeneity and variation in the effect estimates.

A single systematic review found reductions in sepsis, dyspnoea, chest deformity and chest pain with fixation compared to non-operative management. Nevertheless, as the definitions of these were not accurately described it is difficult to know whether the reductions are clinically significant. Reporting of adverse outcomes was infrequent across the reviews, which could reflect lack of measurement and/or reporting of adverse events in the primary studies or the systematic reviews. Therefore there is a risk that without consideration the risks, the benefits of surgery could be overestimated in light of the potential risks. Synthesising multiple meta-analyses data that use the overlapping primary studies has the potential to overestimate the strength of the findings therefore it is important to be mindful of the limited evidence on which our conclusions are based. In addition, significant heterogeneity for several of the outcomes that were pooled makes drawing firm conclusions difficult.

Multiple rib fractures

Evidence in support of multiple rib fracture fixation in the absence of flail chest is limited. Two systematic reviews[15 22] reported on one non-randomised study[31] that recruited between 1996 and 2000, four case series[48-51] and two case reports.[52 53] Hence, due to lack of primary data to synthesise no conclusive statements on effectiveness can be drawn. Only one outcome showed a statistically significant improvement for multiple rib fractures after surgical fixation from one non-randomised study[31] and showed a mean improvement of 4.7 post-operative ventilator days with fixation compared to non-operative management (p=0.02). The only other value reported compared the total ventilator days within this same study[31] and did not show a statistically significant improvement (p=0.12).

Review quality

A significant amount effort and time is required to conduct a high quality systematic review and should only be undertaken when there is sufficient cause[54 55] (e.g. to incorporate the findings of a new RCT or to address an evidence gap). Eight of the systematic reviews were published within 18 months of each other; although none were registered on PROSPERO[56]

so it is possible the authors were unaware of each other's research. Registering reviews allows transparency of methods and also reduces research waste.[57] As similar search strategies and search dates were used in each systematic review inevitably, many of the included studies were the same across reviews.

Only two of the 12 systematic reviews formally appraised the quality of the included studies, therefore 10 of the reviews were not in a position to fully consider the impact of risk of bias on their conclusions. High risk of bias within reviews have affected the conclusions drawn from this evidence synthesis. In a systematic review of 106 emergency surgery systematic reviews, a low risk of bias was found in 53.8% this identifies a common problem of poor quality reviews conducted in emergency surgery.[58]

Heterogeneity and meta-analysis errors

The I^2 value describes the percentage of total variation across studies that is due to heterogeneity rather than chance.[59] Examining the meta-analyses including RCTs highlights moderate to high levels of statistical heterogeneity.

There was also clinical variation in the primary studies in terms of indications and timing of surgery and it is possible that these between study differences could be the cause of the significant heterogeneity. For example, in one RCT[25] patients were randomised after 5 days of invasive ventilation, whereas another RCT[26] randomised and fixed within 24 to 72 hours regardless of initial intubation state. Also, many reviews define the comparator as usual care or non-operative care but do not elaborate on what encompasses this care. Differences in how outcomes were measured may have contributed to between study heterogeneity. It was unknown due to lack of reporting whether the outcomes were equivalent in the pooled primary studies or overall between systematic reviews.

In all systematic reviews with meta-analyses, they reported that two reviewers were involved in the data extraction to minimise errors.[17 19 21 23 24] Despite attempts to minimise errors and therefore an apparent low risk of bias, some errors (up to an MD of 10 days in the

measurement of length of intensive care stay) were identified across reviews. It is worth noting that there were no significant changes in the conclusions drawn from these analyses. Although there was substantial statistical and clinical heterogeneity and lack of consideration of risk of bias in many of the reviews, conclusions tended to be similar and in the direction of benefit with fixation suggesting that further high quality RCTs investigating the effectiveness (including adverse effects) of internal surgical fixation over non-operative management are warranted.

Strengths

Multiple databases were searched for studies and study selection was undertaken by two researchers, reducing the risk of error and bias. Although only English language studies were included, some sources of unpublished studies were searched. It was suspected from the publication dates of seven systematic reviews within 2 years that primary studies could have be synthesised in more than one review therefore a mapping of the studies included in the reviews was undertaken.

Limitations

All systematic reviews were included irrespective of their risk of bias scoring. It could be argued that several reviews were stretching the traditional definition of a systematic review however they did hold to the protocol definition with an electronic database search strategy and included primary evidence. Due to best evidence topics and rapid evidence synthesis being included it was then difficult to apply the ROBIS tool consistently. The ROBIS tool is not designed for rapid evidence synthesis and therefore this type of review showed high risk of bias as they were being assessed against a tool designed for full systematic reviews. Rapid evidence syntheses, by their nature address a trade-off between time and methodological rigour and comprehensiveness.[60]

CONCLUSION

The considerable duplication of work across reviews could be mitigated through protocol registration and greater attention to establishing whether a review is necessary by scoping the literature before commencing a new review. Despite this review identifying 12 systematic reviews they only included 37 unique primary studies, only three of which were RCTs. Synthesis of the reviews has shown some potential improvement in patient outcomes with flail chest after surgical fixation. However, there were differences in indications and timing of surgical fixations in the primary studies and moderate to high levels of heterogeneity across reviews. Further robust evidence is required before conclusions can be drawn of the effectiveness of surgical fixation for flail chest and in particular, multiple rib fractures.

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Contributor statement

HI contributed to conceptualisation, methodology, investigation, formal analysis, original draft preparation. EC contributed to investigation, validation, review and editing. WE contributed to funding acquisition, conceptualisation, review and editing. AR contributed to funding acquisition, conceptualisation, review and editing. CH contributed to methodology, supervision, conceptualisation, review and editing. CM contributed to methodology, investigation, validation, conceptualisation, supervision, review and editing. All authors approve the final version of the manuscript and are accountable for all aspects of the work.

Competing Interests

None declared

Data sharing statement

All data used for the preparation of this review are reported within the manuscript or it's supplementary files.

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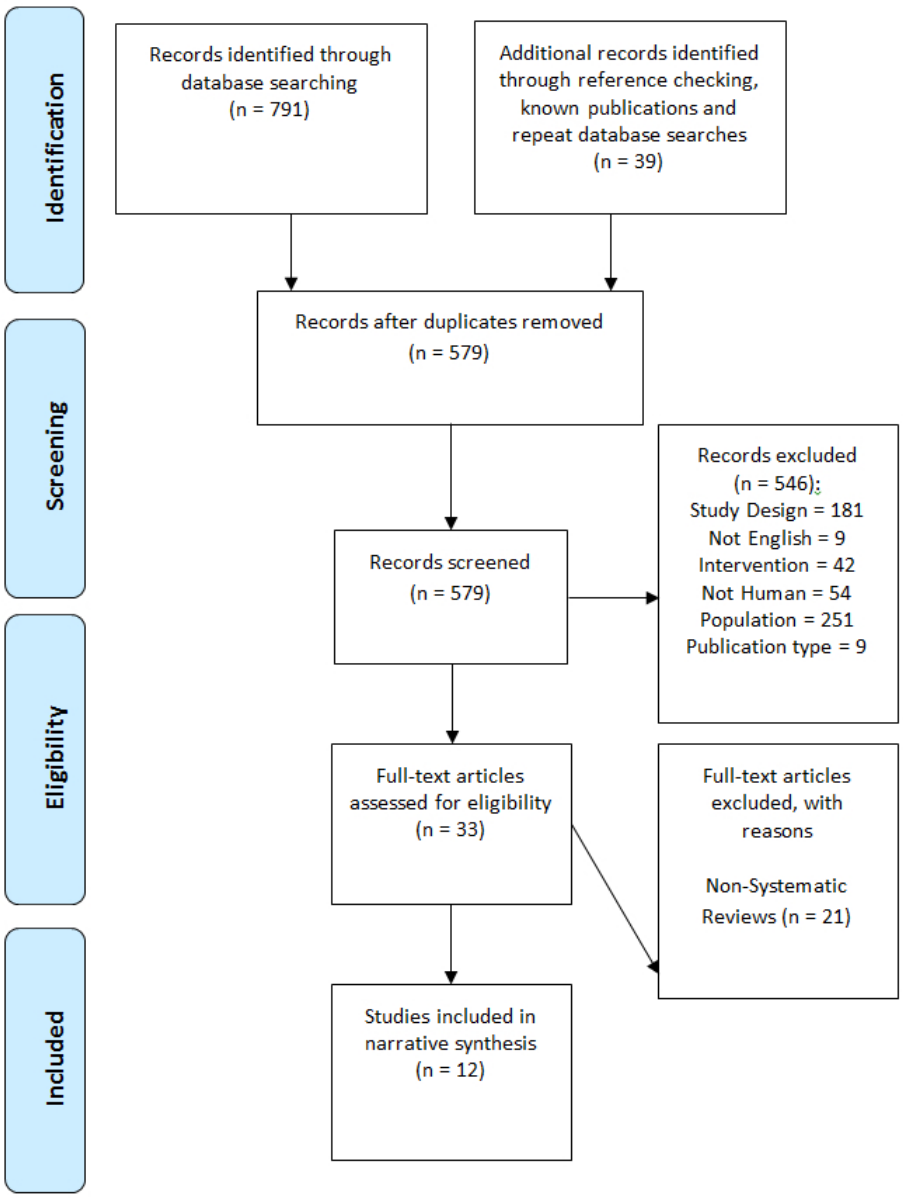
SUPPORTING INFORMATION CAPTIONS

Fig1 PRISMA Flow diagram

Table 1 Review characteristics
Table 2 Primary studies included in each review and the number of included patients
Table 3 Risk of bias using ROBIS tool
Table 4 Results of individual reviews that report a meta-analysis for flail chest
Table 5 Results of individual reviews that report a narrative synthesis for flail chest
Table 6 Results of individual reviews that report a narrative synthesis for multiple rib fractures

S Appendix 1 Medline search strategy

S Appendix 2 Excluded studies



PRISMA Flow diagram

174x225mm (96 x 96 DPI)

Additional file 1 MEDLINE search strategy (OVID interface)

1. (rib adj3 fracture*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

2. ((flail chest or stove? in) adj3 chest).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

3. (blunt chest adj3 trauma).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

4. extra thoracic injur*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

5. costal fracture*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

6. Flail Chest/

7. Rib Fractures/

8. 1 or 2 or 3 or 4 or 5 or 6 or 7

9. (fracture* adj3 fixation).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

10. bone screw*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

11. Bone plate*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

12. (suture adj3 fixation).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

13. judet strut.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

14. bioabsorbable plate*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

15. heavy suture*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

16. intramedullary splint*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

17. (metal adj2 fixation).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

18. ((plate* or strut) adj3 fixation*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

19. exp Internal Fixators/

20. fracture fixation/ or fracture fixation, internal/ or fracture fixation, intramedullary/

21. (fracture adj3 stabili?ation).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

22. 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21

23. 8 and 22

24. limit 23 to (humans and yr="1976 -Current")

Additional content 2 Excluded studies with reasons given for exclusion

1	Galan G, Penalver JC, Paris F, et al. BLUNT CHEST INJURIES IN 1696 PATIENTS. Eur J Cardiothorac Surg. 1992; 6: 284-7.	Study Design
2	Actis Dato GM, Aidala E and Ruffini E. Surgical management of flail chest. Ann Thorac Surg. 1999; 67: 1826-7.	Study Design
3	Ahmed Z and Mohyuddin Z. Management of flail chest injury: Internal fixation versus endotracheal intubation and ventilation. Journal of Thoracic and Cardiovascular Surgery. 1995; 110: 1676-80.	Study Design
4	Akkus M, Utkusavas A, Hanozu M, Kaya M and Bakir I. Stabilization of Flail Chest and Fractured Sternum by Minimally Invasive Repair of Pectus Excavatum. Thoracic and Cardiovascular Surgeon Reports. 2015; 4: 11-3.	Study Design
5	Althausen PL, Shannon S, Watts C, et al. Early surgical stabilization of flail chest with locked plate fixation. J Orthop Trauma. 2011; 25: 641-7.	Study Design
6	Ananiadou O, Karaiskos T, Givissis P and Drossos G. Operative stabilization of skeletal chest injuries secondary to cardiopulmonary resuscitation in a cardiac surgical patient. Interact Cardiovasc Thorac Surg. 2010; 10: 478-80.	Study Design
7	Attia RQ, Schulte KL and Whitaker DC. eReply: In patients with acute flail chest does surgical rib fixation improve outcomes in terms of morbidity and mortality? Interactive Cardiovascular and Thoracic Surgery. 2016; 23: 319-20.	Study Design
8	Bailey J, VanderHeiden T, Burlew CC, et al. Thoracic hyperextension injury with complete "bony disruption" of the thoracic cage: Case report of a potentially life-threatening injury. World Journal of Emergency Surgery. 2012; 7.	Study Design
9	Beelen R, Rumbaut J and De Geest R. Surgical stabilization of a rib fracture using an angle stable plate. Journal of Trauma - Injury, Infection and Critical Care. 2007; 63: 1159-60.	Study Design
10	Beltrami V, Martinelli G, Giansante P and Gentile K. An original technique for surgical stabilisation of traumatic flail chest. Thorax. 1978; 33: 528-9.	Study Design
11	Berthet JP, Solovei L, Tiffet O, et al. Chest-wall reconstruction in case of infection of the operative site: Is there any interest in titanium rib osteosynthesis. Eur J Cardiothorac Surg. 2013; 44: 866-74.	Study Design
12	Bibas BJ and Bibas RA. Operative stabilization of flail chest using a prosthetic mesh and methylmethacrylate. Eur J Cardiothorac Surg. 2006; 29: 1064-6.	Study Design
13	Bille A, Okiror L, Campbell A, Simons J and Routledge T. Evaluation of long-term results and quality of life in patients who underwent rib fixation with titanium devices after trauma. General Thoracic and Cardiovascular Surgery. 2013; 61: 345-9.	Study Design

14	Bille A, Okiror L, Karenovics W and Routledge T. Experience with titanium devices for rib fixation and coverage of chest wall defects. Interactive Cardiovascular and Thoracic Surgery. 2012; 15: 588-95.	Study Design
15	Bonne SL, Turnbull IR and Southard RE. Technique for repair of fractures and separations involving the cartilaginous portions of the anterior chest wall. Chest. 2015; 147: e199-e204.	Study Design
16	Borrelly J and Aazami MH. New insights into the pathophysiology of flail segment: The implications of anterior serratus muscle in parietal failure. Eur J Cardiothorac Surg. 2005; 28: 742-9.	Study Design
17	Bottlang M, Long WB, Phelan D, Fielder D and Madey SM. Surgical stabilization of flail chest injuries with MatrixRIB implants: A prospective observational study. Injury. 2013; 44: 232-8.	Study Design
18	Brotzu G, Montisci R, Pillai W and Sanna S. Chest injuries. A review of 195 patients. Ann Chir Gynaecol. 1988; 77: 155-9.	Study Design
19	Buyukkarabacak YB, Sengul AT, Celik B, et al. The Usefulness of Early Surgical Rib Stabilization in Flail Chest. Acta Chir Belg. 2015; 115: 408-13.	Study Design
20	Cacchione RN, Richardson JD and Seligson D. Painful nonunion of multiple rib fractures managed by operative stabilization. Journal of Trauma - Injury, Infection and Critical Care. 2000; 48: 319-21.	Study Design
21	Campbell N, Conaglen P, Martin K and Antippa P. Surgical stabilization of rib fractures using inion OTPS wraps-techniques and quality of life follow-up. Journal of Trauma - Injury, Infection and Critical Care. 2009; 67: 596-601.	Study Design
22	Caragounis EC, Olsen MF, Pazooki D and Granhed H. Surgical treatment of multiple rib fractures and flail chest in trauma: a one-year follow-up study. World Journal of Emergency Surgery. 2016; 11.	Study Design
23	Chapman BC, Herbert B, Rodil M, et al. RibScore: A novel radiographic score based on fracture pattern that predicts pneumonia, respiratory failure, and tracheostomy. J Trauma Acute Care Surg. 2016; 80: 95-101.	Study Design
24	Charafeddine AH, Stone ME, Reddy SH, Teperman SH, Kaban JM and Cohen-Levy WB. Anterior chest wall disassociation: A pattern associated with serious underlying injury. Am Surg. 2015; 81: E244-E5.	Study Design
25	Cho YH, Kim HK, Kang DY and Choi YH. Reoperative surgical stabilization of a painful nonunited rib fracture using bone grafting and a metal plate. J Orthop Trauma. 2009; 23: 605-6.	Study Design
26	De La Santa Barajas PM, Polo Otero MD, Delgado Sanchez- Gracian C, Leal Ruiloba S, Trinidad C and Choren Duran M. Surgical treatment for flail chest. Interactive Cardiovascular and Thoracic Surgery. 2012; 15: S5.	Study Design
27	De Moya M, Bramos T, Agarwal S, et al. Pain as an indication for rib fixation: A bi-institutional pilot study. Journal of Trauma -	Study Design

	Injury, Infection and Critical Care. 2011; 71: 1750-4.	
28	de Palma A, Sollitto F, Loizzi D, et al. Chest wall stabilization and reconstruction: Short and long-term results 5 years after the introduction of a new titanium plates system. Journal of Thoracic Disease. 2016; 8: 490-8.	Study Design
29	Dean NC, Van Boerum DH and Liou TG. Rib plating of acute and sub-acute non-union rib fractures in an adult with cystic fibrosis: a case report. BMC Res Notes. 2014; 7: 681.	Study Design
30	Defreest L, Tafen M, Bhakta A, et al. Open reduction and internal fixation of rib fractures in polytrauma patients with flail chest. Am J Surg. 2016; 211: 761-7.	Study Design
31	Dehghan N, de Mestral C, McKee MD, Schemitsch EH and Nathens A. Flail chest injuries: A review of outcomes and treatment practices from the National Trauma Data Bank. Journal of Trauma and Acute Care Surgery. 2014; 76: 462-8.	Study Design
32	Doben AR, Eriksson EA, Denlinger CE, et al. Surgical rib fixation for flail chest deformity improves liberation from mechanical ventilation. J Crit Care. 2014; 29: 139-43.	Study Design
33	Dunlop RLE, Tiong W, Veerasingam D and Kelly JL. Novel use of hand fracture fixation plates in the surgical stabilisation of flail chest. Journal of Plastic, Reconstructive and Aesthetic Surgery. 2010; 63: e51-e3.	Study Design
34	Engel C, Krieg JC, Madey SM, Long WB and Bottlang M. Operative chest wall fixation with osteosynthesis plates. Journal of Trauma - Injury, Infection and Critical Care. 2005; 58: 181-6.	Study Design
35	Evman S, Kolbas I, Dogruyol T and Tezel C. A Case of Traumatic Flail Chest Requiring Stabilization with Surgical Reconstruction. Thoracic and Cardiovascular Surgeon Reports. 2015; 4: 8-10.	Study Design
36	Fagevik Olsén M, Pazooki D and Granhed H. Recovery after stabilising surgery for 'flail chest'. Unfallchirurgie. 2013; 39: 501-6.	Study Design
37	Farquhar J, Almahrabi Y, Slobogean G, et al. No benefit to surgical fixation of flail chest injuries compared with modern comprehensive management: results of a retrospective cohort study. Canadian Journal of Surgery. 2016; 59: 299-303.	Study Design
38	Flagel BT, Luchette FA, Reed RL, et al. Half-a-dozen ribs: the breakpoint for mortality. Surgery. 2005; 138: 717-23; discussion 23-5.	Study Design
39	Gabram SGA, Devanney J, Jones D and Jacobs LM. Delayed hemorrhagic pericardial effusion: Case reports of a complication from severe blunt chest trauma. Journal of Trauma. 1992; 32: 794-800.	Study Design
40	Galvin IF, Costa R and Murton M. FRACTURED RIB WITH PENETRATING CARDIOPULMONARY INJURY. Ann Thorac Surg. 1993; 56: 558-9.	Study Design

41	Gardenbroek TJ, Bemelman M and Leenen LPH. Pseudarthrosis of the ribs treated with a locking compression plate: A report of three cases. Journal of Bone and Joint Surgery - Series A. 2009; 91: 1477-9.	Study Design
42	Gasparri MG, Almassi GH and Haasler GB. Surgical management of multiple rib fractures. Chest. 2003; 124: 295S-6S.	Study Design
43	George RJ and Stern HS. An approach to surgical fixation of traumatic costosternal diastasis. ANZ J Surg. 2014; 84: 594-5.	Study Design
44	Gerov I and Yablanski V. Damage control - Increasing the survival rates through emergency bone stabilization in a polytraumatized young patient. Injury. 2011; 42: S29.	Study Design
45	Ginsberg RJ and Kostin RF. 5. New approaches to the management of flail chest. Can Med Assoc J. 1977; 116: 613-5.	Study Design
46	Govaert G, Schuetz M and Peters P. Rib fixation for a traumatic 'stove-in chest': An option to consider. ANZ J Surg. 2012; 82: 276-7.	Study Design
47	Granetzny A, Abd El-Aal M, Emam E, Shalaby A and Boseila A. Surgical versus conservative treatment of flail chest. Evaluation of the pulmonary status. Interact Cardiovasc Thorac Surg. 2005; 4: 583-7.	Study Design
48	Granhed HP and Pazooki D. A feasibility study of 60 consecutive patients operated for unstable thoracic cage. J Trauma Manag Outcomes. 2014; 8: 20.	Study Design
49	Guernelli N, Bragaglia RB, Briccoli A, Mastrorilli M and Vecchi R. Technique for the management of anterior flail chest. Thorax. 1979; 34: 247-8.	Study Design
50	Gunn JM, Savola J and Isotalo K. Left-sided diaphragmatic and pericardial ruptures with subluxation of the heart after blunt trauma. Ann Thorac Surg. 2012; 93: 317-9.	Study Design
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PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	3
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	3
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	4
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4-5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	S1
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	5-6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	6
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	5
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	6

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	6
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	N/A
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	7
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	8-13
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	16-17
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	17-18, 24-25, 27
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	17-33
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	14-16
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	N/A
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	33-34
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	36
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	37
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	37

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A systematic review of systematic reviews for effectiveness of internal fixation for flail chest and rib fractures in adults

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A SYSTEMATIC REVIEW OF SYSTEMATIC REVIEWS FOR EFFECTIVENESS OF INTERNAL FIXATION FOR FLAIL CHEST AND RIB FRACTURES IN ADULTS

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WORD COUNT 3966

ABSTRACT

Objectives

Multiple systematic reviews have reported on the impact of rib fracture fixation in the presence of flail chest and multiple rib fractures, however this practice remains controversial. Our aim is to synthesise the effectiveness of surgical fixation of rib fractures as evidenced by systematic reviews.

Design

A systematic search identified systematic reviews comparing effectiveness of rib fracture fixation with non-operative management of adults with flail chest or multiple rib fractures. MEDLINE, EMBASE, Cochrane Database of Systematic Reviews (CDSR) and Science Citation Index were last searched 17th March 2017. Risk of bias was assessed using the ROBIS tool. The primary outcome was duration of mechanical ventilation.

Results

Twelve systematic reviews were included, consisting of 3 unique randomised controlled trials, 19 non-randomised studies). Length of mechanical ventilation was shorter in the fixation group compared to the non–operative group in flail chest; pooled estimates ranged from -4.52 days, 95% CI [-5.54, -3.5] to -7.5 days, 95% CI [-9.9, -5.5]. Pneumonia, length of hospital and ICU stay all showed a statistically significant improvement in favour of fixation for flail chest; however, all outcomes in favour of fixation had substantial heterogeneity. There was no statistically significant difference between groups in mortality. Two systematic reviews included one non-randomised studies of multiple rib fracture population; due to limited evidence the benefits with surgery are uncertain.

Conclusions

Synthesis of the reviews has shown some potential improvement in patient outcomes with flail chest after fixation. For future review updates, meta-analysis for effectiveness may need to take into account indications and timing of surgery as a subgroup analysis to address clinical heterogeneity between primary studies. Further robust evidence is

required before conclusions can be drawn of the effectiveness of surgical fixation for flail chest and in particular, multiple rib fractures.

Study Registration

PROSPERO ID CRD 42016053494

KEY WORDS

Rib fracture; Flail chest; Multiple rib fractures; Internal fixation; Systematic review; Meta-analysis; Mortality; Mechanical ventilation; Length of hospital stay; Pneumonia

STRENGTHS AND LIMITATIONS OF THIS STUDY

- Multiple databases were searched for studies and study selection was undertaken by two researchers, reducing the risk of error
- Risk of bias of studies was assessed using the ROBIS tool by two researchers
- Primary research within the reviews was mapped to identify if the reviews were based on the same primary evidence
- Reviews were included regardless of risk of bias

INTRODUCTION

Multiple rib fractures (adjacent unifocal fractures) and flail chest (three or more adjacent bifocal rib fractures with paradoxical chest wall movement) have high mortality (18.7%) due to the associated complications of acute respiratory distress syndrome, pneumonia and haemorrhage.[1] Chest trauma accounts for 15% of all trauma admissions[2] most commonly high-energy transfer injury as a result of a road traffic accidents (57.01%) but also from low energy falls (22.96%).[1] Flail chest in particular has a high mortality rate as chest wall disruption causes an increase in the work of breathing for patients who are often in significant pain.

Current treatment options for severe chest injury are mainly supportive, including multimodal analgesia and anaesthesia, as well as non-invasive and invasive ventilation.[3] Surgical fixation is thought to be beneficial to patients with respiratory failure,[4] intractable

pain[5] or if failing to wean from invasive ventilation secondary to chest trauma.[6 7] Fixation has potential to restore chest wall biomechanics and reduce the complications associated with poor ventilation and secretion clearance.[7] Due to the rapidly, albeit heterogeneous, growing evidence base from multiple systematic reviews it is essential to synthesise evidence for this intervention to ascertain safety and efficacy.

This report is part of a wider systematic review to (i) identify and synthesise the evidence of the effectiveness of surgical rib fracture fixation, (ii) evaluate the evidence for indications and timing of fixation, and (iii) identify the outcomes reported in the literature. Systematic reviews and primary studies were eligible for inclusion. This paper maps and synthesises this evidence from systematic reviews assessing the effectiveness of fixation of rib fractures.

METHODS

The review was undertaken systematically using the methods described by the Centre for Reviews and Dissemination.[8] The protocol was registered on PROSPERO and can be accessed at https://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42016053494.

Eligibility criteria

Population

Adults (over 18 years) who have sustained one or more rib fractures following blunt chest trauma, with or without pulmonary contusion were eligible. Single rib fracture, multiple rib fractures and flail chest injuries were included but treated as separate injuries and therefore reported and analysed separately. Patients with penetrating injuries were excluded. Studies of mixed populations with penetrating and non-penetrating injuries were included only if data were presented separately for the two groups. Surgery for chronic non-union was excluded.

Intervention

Any method of internal surgical fixation such as plate or strut fixation; metal or synthetic material including intramedullary splints and suture fixation were eligible for inclusion.

Comparator

External surgical fixation (traction methods, splints and Hoffman style pin and bar fixation) and non-surgical management (such as supportive ventilation, epidural and regional anaesthesia).

Outcomes

All outcomes were eligible (e.g. mortality, pain and pneumonia). The primary outcome of interest was duration of mechanical ventilation due to the close relationship with mortality and morbidity of ventilator associated complications.

Study design:

Inclusion: Systematic reviews were included if they specified a search strategy in at least one literature database and included primary research. No restrictions were placed on the study design of the primary studies.

Exclusion: Literature reviews that did not have a defined research question, search strategy or defined process of selecting articles.

Search strategy

MEDLINE including PreMEDLINE, EMBASE, Cochrane Database of Systematic Reviews (CDSR) and Science Citation Index. Clinical guidance, policy documents and relevant databases such as NICE Evidence, the UK Department of Health policy content, National Clinical Guideline Centre, and Scottish Intercollegiate Guidelines Network (SIGN) were searched on 14 December 2016 and updated on 13 March 2017. The Conference Proceedings Citation Index was also searched for unpublished literature.

The start date for the MEDLINE searches was 1976 as that was the year that Advance Trauma Life Support was introduced internationally, incorporating new methods of resuscitation which have significantly improved outcomes.

The search strategy, developed for MEDLINE, is provided in **Supplementary File 1** and was adapted to run appropriately on other databases. To identify relevant further reviews reference lists of included studies were assessed for eligibility.

Selection

Searches were downloaded into Endnote X7 (Clarivate Analytics, Version 7.1 release date 2/04/2014) and de-duplicated. Two researchers (HI and EC) independently screened titles and abstracts. Any paper classified as potentially eligible by either reviewer was ordered as a full text and independently screened by both reviewers. It was originally planned to have second screening of only 50% but resources allowed for full duplicate screening. A third researcher reviewed disagreements (CM) where a consensus could not be reached between the researchers.

Data extraction

Extracted data included study characteristics, patient characteristics, intervention, comparator, outcome measures, duration of follow up, effect estimates, standard errors (SE) and confidence intervals (CI) as available.

One researcher completed data extraction (HI); a second researcher cross-checked 50% (EC). Discrepancies were cross-checked by both researchers at a second review and a consensus reached.

Risk of bias

Quality assessment with the ROBIS Tool[9] was undertaken by one researcher (HI) and checked by a second (CM). Discrepancies were resolved by discussion.

Data synthesis

All types of internal surgical fixation were synthesised as one group. Flail chest and multiple rib fractures are considered different injuries and were synthesised separately for each outcome extracted. Each outcome was narratively synthesised including number of reviews using the outcome and effect estimates with 95% confidence intervals from the source review. Important numerical data was presented in tables for all outcomes measured. All outcomes that were reported in the reviews were included in the report to avoid reporting bias.[10] Although not fully applicable, reporting was in accordance as much as possible with the PRISMA statement.[11]

Protocol Deviations

The registered protocol encompasses a larger body of work which includes synthesis of primary research for effectiveness, indications for surgery, timing of surgery and mapping of outcome measures. Only the synthesis of systematic reviews is reported here. Although all outcomes were extracted and presented in tables only those that were measured in two or more studies were narratively synthesised.

Patient involvement

Patients were not involved in the preparation or conduct of this review.

RESULTS

Electronic searches identified 791 records; an additional 39 records were collected following reference checking. The full text screening identified 12 systematic reviews eligible for inclusion, there were 21 papers excluded because they were not classified as systematic reviews (Figure 1) .Supplementary File 2 lists the excluded studies.

Review characteristics

Eleven systematic reviews and one rapid evidence synthesis[12], published between 2010 and June 2016, met the inclusion criteria. Table 1 provides a summary of review characteristics. Three of the reviews[13 14 15] were presented as best evidence topics[16]

Table 1 Review characteristics

Review Year Country	Review aim	Search strategy	Studies and participants	PICOS	Risk of bias	Authors' Conclusions
Swart [17] 2016 USA	To perform a meta-analysis of high quality literature to evaluate both economic and medical benefits of early fixation of rib fractures in severe chest trauma	PubMed, Embase, Medline and Scopus, No search start date Last search date 1 June 2016 Search terms defined, No limitations described Evidence of hand searching Eligibility criteria - over 18 years of age and studies comparing operative vs non-operative treatment	3 RCT n =123 14 Case Control 3 Case Series	**Population** Acute flail chest 18 years or old **Intervention** Operative Fixation **Comparator** Non-operative **Studies Type** All study designs	No evidence of quality assessment	Acute ORIF of rib fractures in patients with flail chest injuries results in reduced mortality and medical complications in conjunction with being cost effective intervention.
Schuurmans [18] 2016 Netherlands	Investigate how operative management improves patient care for adults with flail chest.	PubMed, Trip database, Google Scholar No search start date Last search date November 2015 Search terms defined, No limitations described Evidence of reference checking Eligibility criteria - studies comparing operative vs non-operative treatment, RCT only and English	3 RCT n = 123	**Population** Acute flail chest **Intervention** Operative Fixation **Comparator** Non-operative **Studies Type** RCTs	Quality assessment completed but criteria and explanation unclear	The operative management group showed a significant lower incidence of pneumonia, whereas mortality rate did not differ between treatment groups.
Schulte [13] 2016 UK	In patients with acute flail chest does surgical rib fixation improve outcomes in terms of morbidity and mortality?	OVID MEDLINE® Search start date 1946 Last search date January 2016 Search terms defined Search strategy description minimal, No limitations described No evidence of reference checking No specific inclusion or exclusion criteria defined.	1 Meta-analysis by separate author 1 RCT n=123 (2 further coded as RCT which are non-randomised studies) 3 Retrospective cohort studies	**Population** Acute flail chest **Intervention** Operative Fixation **Comparator** Non-operative **Studies Type** Unclear	No evidence of quality assessment	Surgical stabilization of flail chest in thoracic trauma patients has beneficial effects with respect to reduced ventilatory support, shorter intensive care and hospital stay, reduced incidence of pneumonia and septicaemia, decreased risk of chest deformity and an overall reduced mortality when compared with patients

						who received non-operative management.
Coughlin [19] **2016 UK**	Compare the efficacy of flail chest surgical stabilisation to non-operative management	PubMed MEDLINE, Embase, Cochrane Library, clinical trials.gov. No search start date Last search date February 2015 Search terms defined, No limitations Evidence of reference checking Eligibility criteria - studies comparing operative vs non-operative treatment in flail chest and RCT only	3 RCT n = 123	**Population** Traumatic flail chest **Intervention** Surgical stabilisation of any kind **Comparator** Patients treated non-operatively by any other means **Studies Type** RCTs only	Clear quality appraisal of the studies	Surgical stabilisation for a traumatic flail chest is associated with significant clinical benefits including rate of pneumonia, length of hospital an ICU stay and duration of mechanical ventilation in this meta-analysis of three relatively small RCTs
Unsworth [20] **2015 Australia**	To review the treatments for blunt chest trauma and their impact on patient and hospital outcomes. Specifically alludes to surgical stabilization of flail chest.	Cochrane, Medline, EMBASE and CINAHL databases Search limited to 1990 onwards Last search date March 2014 Search terms defined. Limited to humans and adults Evidence of reference checking Eligibility criteria - original research, blunt chest trauma, intervention for blunt chest trauma including a comparator and contained measured outcomes	3 RCT n =123 5 Retrospective Case Controls n= 642 1 Retrospective cohort n = 21	**Population** Adult blunt chest trauma Flail chest **Intervention** Multidisciplinary Intervention (Models of care, management intervention, care practices, care protocols) **Comparator** Other intervention not specified **Studies Type** RCTs	Some quality assessment completed but criteria and explanation unclear	Across the literature there were consistent improvements in patients with flail chest and surgical fixation with fewer days of mechanical ventilation, ICU-LOS and cost savings compared to non-operative techniques. Three out of nine studies were randomized controlled trials, and the level of evidence in all studies was primarily fair or good.
De Lesquen [15] **2015 France**	In flail chest is open reduction and internal fixation needed?	Medline and Science Direct Search start date limited to 1994 onwards Last search date January 2014 Search Terms defined	2 Meta-analysis 3 RCT n = 123 1 prospective cohort n = 60	**Population** Blunt chest trauma. Flail chest **Intervention**	No evidence of quality assessment	For flail chest, early surgical stabilization can be considered in patients who would require mechanical ventilation for >48 h

		No evidence of hand searching or reference checking Eligibility criteria - Exclusions of both child and vascular injuries	5 Retrospective cohort n = 238	Open reduction and internal fixation **Comparator** Unclear **Studies Type** Unclear		
Cataneo [21] 2015 Brazil	To evaluate the effectiveness and safety of surgical stabilization compared with clinical management for people with flail chest	Cochrane Injuries Group Specialised Register, CENTRAL, Medline, Embase, CINAHL, SCI, CPCI-S, Clinical trials.gov, ICTR No search start date Last search Date 12th May 2014. Search terms defined, No limitations Evidence of reference checking Eligibility criteria - RCTs.	3 RCTs n = 123	**Population** Adults or children with flail chest **Intervention** Surgical stabilisation of any kind **Comparator** Clinical management included any type of chest wall stabilization without surgical intervention such as straps or bags and any type of ventilatory assistance. **Studies Type** RCTs only	Clear quality appraisal of the studies	There was no evidence that surgical intervention reduced mortality in people with FC compared with nonsurgical management. There was some evidence that surgical intervention could reduce the risk of developing pneumonia and thoracic deformity; need for tracheostomy; duration of mechanical ventilation, length of ICU stay, and hospital stay; and chronic pain, but the trials to date have been small. There is an urgent need for larger high-quality randomized con-trolled trials.
De Jong [22] 2014 Netherlands	To specify indications for rib fracture fixation of non-flail chests	Medline, Cochrane, Embase Search start date limited to 2010 Last search date December 2013 Search terms defined, limited to year 2000 onwards. Evidence of reference checking Eligibility criteria - Studies included at least 10 participants who were surgically treated for non-flail chest rib fractures. Reported in English, Dutch, or German. Excluded were case reports, biomechanical studies, animal studies, and expert opinions.	1 Case Control n = 60 2 Cohort studies n = 47	**Population** Traumatic non-flail chest **Intervention** Surgical treatment of non-flail chest **Comparator** Unclear **Studies Type**	No evidence of quality assessment	The evidence for surgical treatment of non-flail chest rib fractures is limited

				All studies with at least 10 surgically treated		
Slobogean [23] 2013 Canada	Compare the critical care outcomes of surgical fixation to non-operative management in patients with flail chest injuries	Medline, Embase, Cochrane Database of Systematic Reviews (CDSR), and the Cochrane Central, Register of Controlled Trials (CENTRAL) No search start date Last search date May 2011 No limitations No evidence of reference checking or hand searching Eligibility criteria - Comparator studies with more than 10 cases.	2 RCT 1 case control n= 60 8 Cohort n = 676	**Population** Acute flail chest **Intervention** Operative Fixation **Comparator** Conservative management **Studies Type** RCTs	No evidence of quality assessment	Improved outcomes of multiple critical care outcomes with narrow confidence intervals but based on small retrospective studies. Suggests prospective RCT to overcome potential biases
Leinicke [24] 2013 USA	Comparing operative to non-operative therapy in adult flail chest patients	MEDLINE (1966-2012), Embase (1947-2012), Scopus (all years), Cochrane Databases and ClinicalTrials.gov Last search date February 2012 Search terms defined, limited to English and human studies Evidence of reference checking Eligibility criteria - studies comparing operative vs non-operative treatment in patients with flail chest. Excluded case reports and case series	2 RCT 3 Case Control n=158 4 Cohort n = 303	**Population** Flail chest **Intervention** Operative Fixation **Comparator** Non-Operative **Studies Type** RCTs, cohort, and case-control trials	Clear quality appraisal of the studies	As compared to non-operative therapy, operative fixation of FC is associated with reductions in DMV, LOS, mortality, and complications associated with prolonged MV. These findings support the need for an adequately powered clinical study to further define the role of this intervention
Girsowicz [14] 2012 France	In patients over 45 years old with isolated, movable and painful rib fractures without true flail chest is surgical stabilization superior to non-operative management in improving outcomes?	OVID Medline 1948 –2011 Last search date June 2011 Search terms defined, limited to Human and English language Evidence of reference checking Eligibility criteria – excluded flail chest but inclusions not well described	4 Retrospective cohort n= 107 1 non-systematic Review 1 Case control = 30 2 Case report n= 2	**Population** Over 45 years old with isolated, movable and painful Rib fractures without true flail chest **Intervention** surgical stabilization **Comparator** non-operative management	Some comments on strengths and weaknesses but no quality or risk of bias assessment	Surgical stabilization in the management of isolated multiple non-flail and painful rib fractures improved outcomes (pain, respiratory function, quality of life and reduced socio-professional disability) Studies provided a low level of evidence (small studies with few numbers of patients and short-term follow-up or case reports). Large prospective controlled trials are thus necessary to confirm these encouraging results.

				Studies Type Unclear		
NICE Evidence [12] **2010** **UK**	To make recommendations about the safety and efficacy of surgical rib fracture fixation in flail chest	MEDLINE, PREMEDLINE, EMBASE, Cochrane Library No search start date Last search date May 2010 Search terms defined No limitations No evidence of reference checking but other searches performed Eligibility criteria – clinical studies of patients with flail chest operated with metal rib reinforcements and published in English. Excluded conference abstracts and reviews	1 RCT 2 non randomized studies 4 case series Total 225 patients	**Population** Flail chest **Intervention** Insertion of metal rib reinforcements. **Comparator** Unclear **Studies Type** Clinical studies were included. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded	No evidence of quality assessments	Surgical rib fracture fixation should be consider in patients with flail chest
RCT = Randomised controlled trial, ORIF = Open reduction internal fixation, ICU = Intensive care unit, LOS = Length of stay, FC = Flail chest, MV = Mechanical ventilation, DMV = duration of mechanical ventilation						

Nine reviews[12 13 15 17-19 21 23 24] evaluated the effectiveness of internal surgical fixation in patients with flail chest, two included patients with multiple rib fractures[14 22] and one included all rib fractures but only reported outcomes for flail chest.[20]

Three reviews[18 19 21] included only RCTs and eight included other study designs[12-15 17 22-24] (two systematic reviews, 19 non-randomised studies, 11 case series and two case reports) (Table 2). As would be expected, there was overlap across the reviews in the included primary studies. The total number of patients who had internal fixation in primary studies (excluding duplicate studies) was 1036 and there were 1187 controls.

Table 2 Primary studies included in each review and the number of included patients

	Studies																																		
Review	Leinicke et al. (2013)[25]	Slobogean et al. (2013)[23]	Tanaka (2001)[26]	Granetzny (2005)[27]	Marasco (2013)[28]	Paris (1975)[29]	Kim (1981)[30]	Karev (1997)[31]	Ahmed et al. (1995)[32]	Voggenreiter (1998)[33]	Balci et al. (2004)[34]	Teng (2009)[35]	Nirula et al (2006)[36]	Althausen et al. (2011)[37]	De Moya (2011)[5]	Granhed et al. (2014)[38]	Doben et al. (2014)[39]	Jayle et al. (2015)[40]	Pieracci et al. (2016)[41]	Zhang et al. (2015)[42]	Wada et al. (2015)[43]	Xu et al. (2015)[44]	Majercik (2015)[45]	Defreest (2016)[46]	Ohresser (1972)[47]	Hellberg (1981)[48]	Menard (1983)[49]	Moulton (1997)[50]	Cacchione et al., (2000)[51]	Lardinois (2001)[52]	Kerr -Valentic (2003)[53]	Gasparri et al., (2003)[54]	Borrelly (2005)[55]	Campbell (2009)[56]	Mayberry (2009)[57]	Richardson et al., (2007)[58]	Moreno De La (2010)[59]
Intervention patients			18	20	23	18	18	40	26	20	27	32	30	22	16	60	10	10	35	24	84	17	38	41	14	10	18	23	1	66	40	1	127	32	46	7	22
Control Patients			19	20	23	11	45	93	38	22	37	28	30	28	32	153	11	10	35	15	420	15	57	45	-	-	-	-	-	-	-	-	-	-	-	-	-
Swart [17]			●	●	●		●	●	●	●	●	●	●	●	●	●	●	●		●	●	●	●	●													
Schuurmans[18]			●	●	●																																
Schulte [13]		●												●	●	●	●	●	●	●	●	●															
Coughlin [19]			●	●	●																																
Unsworth [20]			●	●	●				●	●			●	●	●		●																				
de Lesquen [15]	●	●	●	●	●			●	●	●	●		●	●																							
Cataneo [21]																																					
de Jong [22]													●																					●	●		
Slobogean [23]			●	●			●	●	●	●	●	●	●												●								●				
Leinicke [24]			●	●				●		●	●		●	●	●																						
Girsowicz [14]													●																●		●	●		●	●	●	●
NICE [12]			●			●				●																●	●	●		●							
	SR		RCT			Non Randomised Study																			Case Series or Report													

The rapid evidence synthesis by NICE[12] was the first review published in 2010, consisting of seven primary studies including one RCT published in 2001.[26] . Cataneo et al.[21] was the first meta-analysis published (in 2015) and included three RCTs.[26-28] Two further systematic reviews published since then[18 19] identified the same three RCTs and repeated the same meta-analyses for the same review question.

Risk of bias

Seven reviews rated as low risk of bias[12 15 18 19 21 23 24], three as unclear[14 17 22] and two as high.[13 20] (Table 3)The high risk of bias rating was due to lack of detail in the search strategy, no attempts to minimise errors of data extraction and no quality assessment of included studies.

The only review for which a protocol was identified was the Cochrane review undertaken by Cataneo et al.[21]

Table 3 Risk of bias using ROBIS tool

Studies	Study eligibility criteria	Identification and selection of studies	Data collection and study appraisal	Synthesis and findings	Risk of bias in the review
Swart 2016 [17]	Low	Unclear	High	High	Unclear
Schuurmans 2016[18]	Low	Unclear	High	Low	Low
Schulte, 2016 [13]	High	High	High	High	High
Coughlin 2016 [19]	Low	Low	Low	Low	Low
Unsworth 2015 [20]	Low	Low	Unclear	Unclear	High
de Lesquen, 2015 [15]	Unclear	High	Unclear	Unclear	Low
Cataneo, 2015 [21]	Low	Low	Low	Low	Low
de Jong, 2014 [22]	High	Unclear	High	High	Unclear
Slobogean, 2013 [23]	Low	Low	High	Low	Low
Leinicke, 2013 [24]	Low	Low	Low	Low	Low
Girsowicz, 2012 [14]	High	High	High	High	Unclear
NICE Evidence, 2010 [12]	Low	Unclear	Unclear	Low	Low

Outcome evaluation

All reviews undertook a narrative synthesis with six also including a meta-analysis.[17-19 21 23 24] Table 4 summarises the meta-analyses for flail chest; Table 5 summarises the narrative syntheses for flail chest; and Table 6 the narrative syntheses for multiple rib fractures.

Across all the reviews eighteen outcomes were reported and eleven outcomes were reported by more than one review.

Primary outcome - Length of mechanical ventilation (days)

Flail Chest

Ten systematic reviews reported length of mechanical ventilation; six undertook a meta-analysis[17-19 21 23 24] four[17-19 21] of which included the same three RCTs.[26-28]

There was substantial variation across the reviews in the pooled estimates for this outcome, related to pooling different sets of studies. The largest reduction in duration of mechanical ventilation when surgery is compared to no surgery was reported by Slobogean et al.[23] pooling two RCTs[26 27] and six non-randomised studies [30 31 33-36] (Mean difference (MD) -7.5 days, 95% CI [-9.9,-5.5]); (Table 4). The MD was 3 days greater than the pooled estimates from Leinicke et al.[24] (-4.52 days, 95% CI [-5.54, -3.50]) and Swart et al.[17](-4.57 days, SD [0.59]).

Table 4 Results of individual reviews that report a meta-analysis for flail chest

Studies reporting outcome	N of studies (n of participants in analysis)	Study Types		Details of meta-analysis	Results	I^2
		RCT	NR			
Total length of invasive mechanical ventilation (Days)						
Cataneo [21]	3 (123)	3	0	MD [IV, Fixed, 95% CI]	Results not pooled	-
Coughlin [19]	3 (123)	3	0	MD [IV, Random, 95% CI]	-6.30 [-12.16, -0.43]	95
Leinicke [24]	8 (474)	2	6	MD [IV, Random 95% CI]	−4.52 [−5.54, −3.50]	48.6
Schuurmans [18]	3 (123)	3	0	MD [IV, Random, 95% CI]	−6.53 [−11.88, −1.18]	93
Slobogean [23]	8 Studies (563)	2	6	MD [IV, Fixed, 95% CI]	-7.5 [-9.9, -5.0]	48
Swart [17]	18 Studies (1150)	3	15	MD [IV, Random, SD]	-4.57 [0.59]	83
Mortality (frequency)						
Cataneo [21]	3 (123)	3	0	RR [M-H, Fixed, 95% CI]	0.56 [0.13, 2.42]	0
Coughlin [19]	2 (86)	2	0	RR [M-H Random 95% CI]	0.57 [0.13, 2.52]	0
Leinicke [24]	5 (343)	1	0	RR [95% CI]	0.43 [0.28, 0.69]	0
Schuurmans [18]	2 (86)	2	0	RR [M-H, Fixed, 95% CI]	0.56 [0.13, 2.42]	0
Slobogean [23]	7 (582)	2	5	OR [M-H, Fixed, 95% CI]	0.31 [0.20, 0.48]	-
Slobogean [23]	7 (582)	2	5	RR [M-H, Fixed, 95% CI]	0.19 [0.13, 0.26]	0
Swart [17]	13(1263)	3	10	RR [M-H, Random, SD]	0.44 [0.09]	0
Total length of stay in intensive care unit (Days)						
Cataneo [21]	2 (77)	2	0	MD [IV, Fixed, 95% CI]	Results not pooled	-
Coughlin [19]	3 (123)	3	0	MD [IV, Random, 95% CI]	-6.46 [-9.73, -3.19]	35
Leinicke [24]	5 (235)	2	3	MD [IV, Random, 95% CI]	−3.4 [−6.01, −0.80]	74.9
Schuurmans [18]	3 (123)	3	0	MD [IV, Fixed, 95% CI]	−5.18 [−6.17, −4.19]	40
Slobogean [23]	4 (261)	2	2	MD [IV, Fixed, 95% CI]	-4.8 [-7.9, -1.6]	0.1
Swart [17]	14 (840)	3	11	MD [IV, Random, SD]	-3.25 [1.29]	91
Total length of stay in hospital (Days)						
Coughlin [19]	2 (86)	2	0	MD [IV, Random, 95% CI]	-11.39 [-12.39, -10.38]	0
Leinicke [24]	5 (262)	1	4	MD [IV, Random 95% CI]	−3.83 [−7.12, −0.54]	68.9
Schuurmans [18]	2 (86)	2	0	MD [IV, Fixed, 95% CI]	−11.39 [-12.39, −10.38]	0
Slobogean [23]	4 (404)	1	3	MD [IV, Fixed, 95% CI]	-4.0 [-7.4, -0.7]	33
Swart [17]	11(438)	1	10	MD [IV, Random, SD]	-4.48 [1.98]	89

Pneumonia (frequency)						
Cataneo [21]	3 (123)	3	0	RR [M-H Random 95% CI]	0.36 [0.15, 0.85]	66
Coughlin [19]	3 (123)	3	0	RR [M-H Random 95% CI]	0.36 [0.15, 0.85]	66
Leinicke [24]	4 (260)	1	3	RR [95% CI]	0.43 [0.28, 0.69]	31
Schuurmans [18]	2 (83)	2	0	RR [M-H, Fixed, 95% CI]	0.45 [0.29, 0.7]	74
Slobogean [23]	8 (816)	2	6	OR [M-H, Fixed, 95% CI]	0.18 [0.11, 0.32]	4
Slobogean [23]	8 (816)	2	6	RR [M-H, Fixed, 95% CI]	0.31 [0.21, 0.41]	4
Swart [17]	15 (1005)	3	12	RR [M-H, Random, SD]	0.59 [0.10]	55
Tracheostomy (frequency)						
Cataneo [21]	2 (83)	2	0	RR [M-H Random 95% CI]	0.38 [0.14, 1.02]	64
Leinicke [24]	4 (215)	1	3	RR [95% CI]	0.25 [0.13, 0.47]	0
Schuurmans [18]	2 (83)	2	0	RR [M-H, Fixed, 95% CI]	0.4 [0.2, 0.7]	Not reported
Slobogean [23]	3 (165)	1	2	OR [M-H, Fixed, 95% CI]	0.12 [0.04, 0.32]	0
Slobogean [23]	3 (165)	1	2	RR [M-H, Fixed, 95% CI]	0.34 [0.10, 0.57]	0
Swart [17]	11 (975)	2	9	RR [M-H, Random, SD]	0.52 [0.07]	42
Sepsis (frequency)						
Slobogean [23]	4 (345)	0	4	OR [M-H, Fixed, 95% CI]	0.36 [0.19, 0.71]	0
Slobogean [23]	4 (345)	0	4	RR [M-H, Fixed, 95% CI]	0.14 [0.56, 0.23]	0
Spirometry (percentage of predicated)						
Coughlin [19]	-	-	-	-	-	-
FVC	2 (74)	2	0	MD [IV, Random, 95% CI] p-value	1.53 [-13.49, 16.55] p = 0.84	Not reported
FEV1	2 (74)	2	0	MD [IV, Random, 95% CI] p-value	-0.42 [-4.83, 3.98] p = 0.85	Not reported
TLC	2 (74)	2	0	MD [IV, Random, 95% CI] p-value	3.69 [-3.08, 10.46] p = 0.29	Not reported
PEFR	2 (74)	2	0	MD [IV, Random, 95% CI] p-value	0.38 [-0.76, 1.53] p = 0.51	Not reported
Chest deformity (frequency)						
Cataneo [21]	2 (86)	2	0	RR [M-H, Fixed, 95% CI]	0.13 [0.03, 0.67]	0
Slobogean [23]	4 (228)	1	3	OR [M-H, Fixed, 95% CI]	0.11 [0.02, 0.60]	2.1
Slobogean [23]	4 (228)	1	3	RR [M-H, Fixed, 95% CI]	0.30 [0.00,0.60]	2.1
Dyspnoea (frequency)						
Slobogean [23]	3 (135)	1	2	OR [M-H, Fixed, 95% CI]	0.40 [0.16, 1.01]	0

Slobogean [23]	3 (135)	1	2	RR [M-H, Fixed, 95% CI]	0.15 [0.09, 0.39]	0
Chest pain (frequency)						
Slobogean [23] Slobogean [23]	2(71) 2(71)	1 1	1 1	OR [M-H, Fixed, 95% CI] RR [M-H, Fixed, 95% CI]	0.40 [0.01, 12.60] 0.18 [0.46, 0.83]	0 0
RCT= Randomised controlled trial, NR = Non randomised study, RR = Risk ratio, OR = Odds ratio, MD = Mean difference, SD = Standard deviation, CI = Confidence interval, IV - Inverse variance, M-H - Mantel-Haenszel, FVC = Force vital capacity, FEV1 = Forced expiratory volume, TLC = Total lung capacity, PEFR = Peak expiratory flow rate						

There were differences in the data reported across the four meta-analyses[17-19 21] that included the same three RCTs. Schuurmans et al.[18] extracted median duration from the Marasco et al. RCT,[28] producing an estimate MD -6.53 days, 95% CI [-11.88, -1.18]) In contrast, Coughlin et al.[19], Cataneo et al.[21] and Swart et al.[17] report the total mean time on mechanical ventilation, which they state, was obtained directly from the authors producing an estimate MD -6.30 days, 95% CI [-12.16, -0.43]).

Variations also arose in relation to the extraction of data from the RCT by Granetzny et al.[27] who did not report standard deviations (SDs) for mechanical ventilation. Slightly different SD values are found in all six meta-analyses[17-19 21 23 24] which may have arisen from different methods of imputation and all give slightly different estimates.

Substantial heterogeneity was seen in all meta-analyses reporting this outcome[18 19 23 24] (I^2 = 48% to 95%). Only one study[21] did not pool due to heterogeneity.

Narrative synthesis from two reviews concluded that surgery reduces the length of mechanical ventilation compared to no surgery.[15 20] (Table 5)

Table 5 Results of individual reviews that report a narrative synthesis for flail chest

Study details	Included studies	Outcomes assessed	Narrative Synthesis
Author Unsworth [20] **Year** 2015 **Country** Australia	RCT = 2 Granetzny (40) Tanaka (37) Marasco (46) Non randomised= 6 Ahmed (64) Althausen (50) Doben (21) De Moya (48) Nirula (60) Voggenreiter (42) Total number of patients = 408	• Mortality • Pneumonia • Pneumothorax and haemothorax • Hospital length of stay • ICU stay • Costings • Treatment outcome	• Significant decrease in mechanical ventilation requirements after surgical fixation. decreasing in ventilator-acquired pneumonia after surgical fixation • decrease in ICU-LOS, fewer days of mechanical ventilation and cost savings compared to non-operative management • decreased days of ventilator dependence, and shorter ICU-LOS • lower incidence of pneumonia, a higher return to full time work at six months • less persistent pain at six and 12 months in those receiving surgery • significantly fewer days of mechanical ventilation and a shorter hospital and ICU-LOS • The estimated cost savings ranged from US Dollars 10,000 to AU Dollars 14,443 per patient with surgical rib fixation as a result of the decrease in ICU-LOS. • None of the studies were large enough to draw conclusions on the effect of this intervention on thromboembolism and death.
Author de Lesquen [15] **Year** 2015 **Country** France	Meta-analysis = 2 Leinicke 9 studies (538 patients) Slobogean 11 studies (732 patients) RCT = 3 Marasco (46) Granetzny (40) Tanaka (37) Non-randomised= 6 Ahmed (64) Karev (40) Voggenreiter (20) Balci (64) Nirula (60) Althausen (50) Total number of patients=421	• Duration of IMV • LOS ICU • Pneumonia • Mortality	For flail chest, early surgical stabilization can be considered in patients who would require mechanical ventilation for >48 h (Grade B, extrapolated recommendations from Level I evidences).

Author NICE [12] **Year** 2010 **Country** UK	RCT = 1 Tanaka (37) Non-randomised = 2 Voggenreiter (42) Paris (29) Case Series = 4 Lardinois (66) Mouton (23) Menard (18) Hellberg (10) Total number of patients=225 Intervention group = 173 Control group = 52	• Duration of IMV • Mortality • LOS ICU • Pneumonia • Lung function • Return to Employment • Sepsis • Pain or discomfort requiring removal of plates	Surgical stabilisation with metal rib reinforcements aims to allow earlier weaning from mechanical ventilation, reduce acute complications and avoid chronic pain sometimes associated with permanent malformation of the chest wall. Kirschner wire may be used on its own, but this method of rib stabilisation is not covered by this guidance.
Author Schulte [13] **Year** 2016 **Country** UK	Systematic Review = 1 Slobogean (753) RCT = 1 Marasco (23,23) Non-randomised studies = 9 Jayle (10,10) Pieracci (35,35) Zhang (24,15) Wada (84,336) Granhed (60,153) Doben (10,11) Xu (17,15) Althausen (22,28) De Moya (16,32) Total number of patients=1712 Intervention group = 301 Control group = 658	• Duration of IMV • Mortality • LOS hospital • LOS ICU • Pneumonia	Surgical stabilization of flail chest in thoracic trauma patients has beneficial effects with respect to reduced ventilatory support, shorter intensive care and hospital stay, reduced incidence of pneumonia and septicaemia, decreased risk of chest deformity and an overall reduced mortality when compared with patients who received non-operative management.
ICU = Intensive care unit, IMV = invasive mechanical ventilation, LOS = Length of stay, RCT = Randomised controlled trial			

Multiple rib fractures

Two reviews[14 22] included one primary study[36] that had matched non-operative controls[36] (non-operative treatment not described) and reported a statistically significant reduction in post-operative ventilator days ($p = 0.02$) in favour of the fixation group (Table 6) but no statistically significant difference in total ventilator days ($p = 0.12$).

Table 6 Results of individual reviews that report a narrative synthesis for multiple rib fractures

Study details	Included studies	Outcomes assessed	Narrative Synthesis
Author de Jong [22] **Year** 2014 **Country** Netherlands	RCT = 0 Non-randomised = 1 Nirula (60) Case Series = 2 Campbell (32) Mayberry (46, 15 non-flail) Total number of patients=138 Intervention group = 108 Control group = 30	• LOS hospital • Duration of IMV • Time of operation • Chronic pain	Only Nirula et al. concluded that rib fracture fixation showed a trend toward fewer total ventilator days. Mayberry et al. investigated the quality of life after rib fixation, and they concluded that there was low long-term morbidity and pain. Campbell et al. demonstrated low levels of pain and satisfactory rehabilitation.
Author Girsowicz [14] **Year** 2012 **Country** France	Non-systematic review =1 Nirula and Mayberry Case Comparator = 1 Nirula (30,30) Case Series = 4 Mayberry (46) Richardson (7) Barajas (22) Campbell (32) Case report = 3 Gasparri (1) Cacchione (1) Kerr-Valentic (1) Total number of patients=169 Intervention group = 139 Control group = 30	• Pain • Disability • Respiratory function • Number of days lost from work	In general, of the nine studies presented, all indicated that surgical stabilization in the management of isolated multiple non-flail and painful rib fractures improved outcomes. Indeed, the interest and benefit was shown not only in terms of pain and respiratory function but also in improved quality of life and reduced socio-professional disability. Hence, the current evidence shows surgical stabilization to be safe and effective in alleviating post-operative pain and improving patient recovery, thus enhancing the outcome of the procedure. However, retrieved studies provided a low level of evidence (small studies with few numbers of patients and short-term follow-up or case reports). Large prospective controlled trials are thus necessary to confirm these encouraging results.
IMV = invasive mechanical ventilation, RCT = Randomised controlled trial			

Mortality

Flail Chest

Seven reviews reported mortality; six undertook a meta-analysis[17-19 21 23 24 15]. Three reviews[18 19 21] which pooled the same three RCTs[26-28] showed a non-statistically significant reduction in mortality with surgery compared to no surgery (Risk Ratio (RR) 0.56, 95% CI [0.13, 2.42][18 21] and RR 0.57, 95% CI [0.13, 2.52][19] (Table 4)).

Three reviews pooled randomised and non-randomised studies.[17 23 24] Estimates were RR 0.19, 95% CI [0.13, 0.26],[23] (RR 0.43, 95% CI [0.28, 0.69][24] and RR 0.44, SD [0.09][17] Overall, statistical heterogeneity was low (I^2=0%) for this outcome in all studies that presented this data.[17-19 21 23 24]

Multiple rib fractures

Mortality was not assessed by de Jong et al.[22] or Girsowicz et al.[14]

Length of ICU Stay (days)

Flail Chest

Eight reviews[12 15 17-19 21 23 24] assessed length of ICU stay; six undertook a meta-analysis.[17-19 21 23 24] Pooled estimates ranged from -3.25 days [SD 1.29][17] to -6.46 days, 95% CI [-9.73, -3.19][19] and were all in favour of surgical fixation compared to a variety of comparators (Table 4). The range in pooled estimates may be partly explained by the pooling of different sets of studies. However, differences occurred as some pooled median length of ICU stay and others pooled the mean. Furthermore, some used postoperative time spent in ICU and others the total time spent in ICU.[17-19]

Variation also arose across reviews in the data extracted from a trial that did not report SDs in the primary publication.[27] Values were imputed or the raw data obtained from the authors resulting in SD values ranging from 0.7 to 4.4 and 2.2 to 7.3 in the operative and non-operative groups respectively. There was also a substantial difference in the effect estimate for this trial.[27] In one review[24], the effect estimate of -10 days, 95% CI [-15.41, -4.59], was

five days greater than the estimate used from the same trial in other reviews. It is the same as the as length of mechanical ventilation effect estimate reported in the same study[27] so is possibly a transcription error.

Statistical heterogeneity ranged from substantial to none[60] (I^2 = 74.9%[24], 40%[18], 35%[19] and 0.1%[23]). The narrative syntheses concluded that in patients with flail chest undergoing surgical fixation length of ICU stay was reduced compared to non-operative management.[15 20]

Multiple rib fractures

A single review[14] included one non-randomised study reporting no statistically significant difference in ICU days (p =0.51), the MD and 95% CI was not reported [36].

Length of Hospital Stay (days)

Flail Chest

Nine reviews[12 15 17-21 23 24] reported length of hospital stay, six undertook a meta-analysis.[17-19 21 23 24] Two reviews[17 21] pooled the same two trials[26 27] and found a significantly shorter hospital length of stay in favour of surgery compared to non-operative management (MD -11.39 days 95% CI [-12.39, -10.38]). When non-randomised studies were included in the meta-analysis the pooled effects were smaller -3.83 days, 95% CI [-7.12,-0.54],[24] -4 days, 95% CI [-7.4, -0.7][23] and -4.48 days, SD [1.9][17] in favour of fixation; Table 4).

Heterogeneity ranged from low (I^2 = 0[18 19], meta-analyses of RCTs only) to moderate or substantial, (I^2 = 89%,[17] I^2 = 68.9%[24] and I^2 = 33%[23]).

Multiple rib fractures

Two systematic reviews[14 22] (Table 6) included a single non-randomised study[36] reporting no statistically significant difference in hospital stay with surgery (mean 18.8 days [SD 1.8]) compared to the non-operative management (21.1 days [SD 3.9]), (p=0.59).

Pneumonia

Flail Chest

Ten reviews[12 15 17-19 21 23 24 61], reported the risk of developing pneumonia, six undertook a meta-analysis.[13 17-21 23 24] Three RCTs[26-28] were pooled in two of the reviews[15 17] and they found a RR of 0.36, 95% CI [0.15, 0.85], in favour of fixation compared to non-operative management. When non-randomised studies were combined the RR ranged from 0.31, 95% CI [0.21, 0.41][23] to 0.45, 95% CI [0.29, 0.70][25] in favour of fixation (Table 4). Substantial heterogeneity was seen in meta-analyses for this outcome[18 19 21] that included the three RCTs[26-28] (I^2 = 66% to 74%). In the reviews that pooled the RCTs alongside the non-randomised studies[23 24] there were lower levels of heterogeneity (I^2 = 4% and I^2 = 31%, respectively).

Two narrative syntheses report that among patients with flail chest, risk of pneumonia was reduced in the surgery group compared to the no surgery group (Table 5).[15 20]

Tracheostomy

Flail Chest

Five reviews reported a meta-analysis for tracheostomy.[17 18 21 23 24] Pooled RRs ranged from 0.25, 95% CI [0.13, 0.47] to 0.40, 95% CI [0.2, 0.7] (Table 4).Moderate and substantial heterogeneity was seen in two reviews (I^2=42%[17], I^2=64% [21]), low in two reviews [23 24] (I^2=0%), and one did not report heterogeneity. [18]

Sepsis

Flail Chest

One review[23], pooling four non-randomised studies[30 32 33 55] estimated a RR of 0.14, 95% CI [0.56, 0.23] with I^2=0% in favour of fixation compared to non-operative management for sepsis. The estimate RR reported is not possible given the confidence interval does not include the estimated value, 0.14. The lower interval of 0.56 could possibly be -0.56 creating a wider CI and would suggest that the author's conclusion was correct and there was a statistically significant difference in favour of fixation.

Spirometry

Flail Chest

One review[19] reported a meta-analysis of spirometry data which included two RCTs[27 28] with spirometry measured at two different time points (three and two months respectively). No statistically significant differences in any spirometry data were seen between surgery and no surgery (Table 4).

Chest Deformity

Flail Chest

Two reviews reported a meta-analysis of chest deformity[23 21], both reported a statistically significant difference in favour of surgery compared to no surgery (RR 0.30, 95% CI [0.00, 0.60], I^2=2.1% and RR 0.13, 95% CI [0.03 to 0.67], I^2=0%).

Dyspnoea

Flail chest

One review[23] pooled an RCT[26] and two non-randomised studies.[32 47] for dyspnoea (risk ratio 0.15, 95% CI [0.09 to 0.39] in favour of fixation). Duration of follow-up was one year for two of the primary studies[47 26] and unclear in the third.[32] It was unclear how dyspnoea was measured or defined in the three primary studies.

Chest Pain

Flail chest

Chest pain was reported in one review[23] which pooled one RCT[26] and one non-randomised study[47]suggesteing a benefit in favour of fixation (RR 0.18, CI 95% [0.46, 0.83]).

Other reported outcomes

Several other outcomes were reported within the systematic reviews however no others have been pooled in a meta-analysis. A narrative synthesis was not completed on the outcomes: wound infection, pain-requiring removal of metalwork, return to work, socio-

professional disability cost, pulmonary embolism, pneumothorax and haemothorax. In the reviews, data on these additional outcomes was minimal and presented as a narrative synthesis without presenting numerical data (Table 5 and Table 6).

DISCUSSION

Twelve systematic reviews on the effectiveness of surgery for flail chest and multiple rib fractures published between 2010 and 2016. This is the first systematic review of reviews and highlighted that there are a large number of reviews with same aims and including the same primary studies.

Flail chest

Six[17-19 21 23 24] of the 12 systematic reviews presented meta-analyses for flail chest based on overlapping primary studies. They reported reductions in length of mechanical ventilation, length of stay, pneumonia and tracheostomy rates with surgery compared to non-surgical management and inconsistent results for mortality. Across many of the meta-analyses there was moderate to high levels of heterogeneity and variation in the effect estimates.

A single systematic review found reductions in sepsis, dyspnoea, chest deformity and chest pain with surgery compared to no surgery management. Nevertheless, as the outcome measures were not defined it is difficult to know whether the reductions are clinically significant. Reporting of adverse outcomes was infrequent across the reviews, which could reflect lack of measurement and/or reporting of adverse events in the primary studies or the systematic reviews. Therefore, the benefits of surgery could be overestimated in light of the potential risks not being considered. Synthesising multiple meta-analyses data that include overlapping primary studies has the potential to overestimate the strength of the findings therefore it is important to be mindful of the limited evidence on which our conclusions are based. In addition, significant heterogeneity for several of the outcomes that were pooled makes drawing firm conclusions difficult.

Multiple rib fractures

Evidence in support of multiple rib fracture fixation in the absence of flail chest is limited. Two systematic reviews[14 22] reported on one non-randomised study[36] that recruited between 1996 and 2000, four case series[56-59] and two case reports.[51 54] Hence, due to limited evidence no conclusive statements on effectiveness can be drawn.

Review quality

A significant amount of effort and time is required to conduct a high quality systematic review and should only be undertaken when there is sufficient cause[62 63] (e.g. to incorporate the findings of a new RCT or to address an evidence gap). Eight of the systematic reviews were published within 18 months although none were registered on PROSPERO[64] so it is possible the authors were unaware of each other's research. Registering reviews allows transparency of methods and also reduces research waste.[65] As similar search strategies and search dates were used in each systematic review, inevitably many of the included studies were the same across reviews.

Only two of the 12 systematic reviews formally appraised the quality of the included studies, therefore 10 of the reviews were not in a position to fully consider the impact of risk of bias on their conclusions. High or unclear risk of bias within reviews have affected the conclusions drawn from this evidence synthesis. In a systematic review of 106 emergency surgery systematic reviews, a low risk of bias was found in 53.8%, identifying a common problem of poor quality reviews conducted in emergency surgery.[66]

Heterogeneity and meta-analysis errors

The I^2 value describes the percentage of total variation across studies that is due to heterogeneity rather than chance.[67] Examining the meta-analyses including RCTs highlights moderate to high levels of statistical heterogeneity.

There was also clinical variation in the primary studies in terms of indications and timing of surgery and it is possible that these between study differences could be a source of the

substantial heterogeneity. For example, in one RCT[26] patients were randomised after 5 days of invasive ventilation, whereas another RCT[27] randomised and fixed within 24 to 72 hours regardless of initial intubation state. Also, many reviews define the comparator as usual care or non-operative care but do not elaborate on what encompasses this care. Differences in how outcomes were measured may also have contributed to between study heterogeneity. It was unknown due to lack of reporting whether the outcomes were equivalent in the pooled primary studies or overall between systematic reviews.

In all systematic reviews with meta-analyses, they reported that two reviewers were involved in the data extraction to minimise errors.[17 19 21 23 24] Despite attempts to minimise errors and therefore an apparent low risk of bias, some errors (up to an MD of 10 days in the measurement of length of intensive care stay) were identified across reviews. It is worth noting that there were no significant changes in the conclusions drawn from these analyses. Although there was substantial statistical and clinical heterogeneity and lack of consideration of risk of bias in many of the reviews, conclusions tended to be similar and in the direction of benefit with fixation suggesting that further high quality RCTs investigating the effectiveness (including adverse effects) of internal surgical fixation over non-operative management are warranted.

Strengths

Multiple databases were searched for studies and study selection was undertaken by two researchers, reducing the risk of error and bias. Although only English language studies were included, some sources of unpublished studies were searched. A mapping of the studies included in the reviews was undertaken to take into account individual studies being included in multiple reviews and hence double counting studies.

Limitations

All systematic reviews were included irrespective of their risk of bias scoring. It could be argued that several reviews were stretching the traditional definition of a systematic review

however they did hold to the protocol definition with an electronic database search strategy and included primary evidence. Due to best evidence topics and rapid evidence synthesis being included it was then difficult to apply the ROBIS tool consistently. The ROBIS tool is not designed for rapid evidence synthesis and therefore this type of review showed high risk of bias as they were being assessed against a tool designed for full systematic reviews. Rapid evidence syntheses, by their nature address a trade-off between time and methodological rigour and comprehensiveness.[68]

CONCLUSION

The considerable duplication of work across reviews could be mitigated through protocol registration and greater attention to establishing whether a review is necessary by scoping the literature before commencing a new review. Despite this review identifying 12 systematic reviews they only included 37 unique primary studies, only three of which were RCTs. Synthesis of the reviews has shown some potential improvement in patient outcomes with flail chest after surgical intervention. However, there were differences in indications and timing of interventions in the primary studies and moderate to high levels of heterogeneity across reviews. For future review updates, meta-analysis for effectiveness may need to take into account indications and timing of surgery as a subgroup analysis to address clinical heterogeneity between primary studies. Further robust evidence is required before conclusions can be drawn of the effectiveness of surgical fixation for flail chest and in particular, multiple rib fractures.

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Contributor statement

HI contributed to conceptualisation, methodology, investigation, formal analysis, original draft preparation. EC contributed to investigation, validation, review and editing. WE contributed to conceptualisation, review and editing. AR contributed to funding acquisition, conceptualisation, review and editing. CH contributed to methodology, supervision, conceptualisation, review and editing. CM contributed to methodology, investigation, validation, conceptualisation, supervision, review and editing. All authors approve the final version of the manuscript and are accountable for all aspects of the work.

Competing Interests

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Data sharing statement

All data used for the preparation of this review are reported within the manuscript or its supplementary files.

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50. Mouton W, Lardinois D, Furrer M, et al. Long-term follow-up of patients with operative stabilisation of a flail chest. *Thorac Cardiovasc Surg* 1997;45(5):242-4.
51. Cacchione RN, Richardson JD, Seligson D. Painful nonunion of multiple rib fractures managed by operative stabilization. *Journal of Trauma - Injury, Infection and Critical Care* 2000;48(2):319-21.
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56. Campbell N, Conaglen P, Martin K, et al. Surgical stabilization of rib fractures using inion OTPS wraps-techniques and quality of life follow-up. *Journal of Trauma - Injury, Infection and Critical Care* 2009;67(3):596-601. doi: http://dx.doi.org/10.1097/TA.0b013e3181ad8cb7
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62. Garner P, Hopewell S, Chandler J, et al. When and how to update systematic reviews: consensus and checklist. *BMJ* 2016;354 doi: 10.1136/bmj.i3507
63. Lund H, Juhl C, Christensen R. Systematic reviews and research waste. *The Lancet*;387(10014):123-24. doi: 10.1016/S0140-6736(15)01354-9
64. Booth A, Clarke M, Dooley G, et al. The nuts and bolts of PROSPERO: an international prospective register of systematic reviews. *Systematic Reviews* 2012;1:2-2. doi: 10.1186/2046-4053-1-2
65. Moher D, Booth A, Stewart L. How to reduce unnecessary duplication: use PROSPERO. *BJOG: An International Journal of Obstetrics & Gynaecology* 2014;121(7):784-86. doi: 10.1111/1471-0528.12657
66. EMSurg Collaborators. Methodological overview of systematic reviews to establish the evidence base for emergency general surgery. *Br J Surg* 2017;104(5):513-24. doi: 10.1002/bjs.10476 [published Online First: 2017/03/16]
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68. Featherstone RM, Dryden DM, Foisy M, et al. Advancing knowledge of rapid reviews: an analysis of results, conclusions and recommendations from published review articles examining rapid reviews. *Syst Rev* 2015;4:50. doi: 10.1186/s13643-015-0040-4 [published Online First: 2015/05/01]

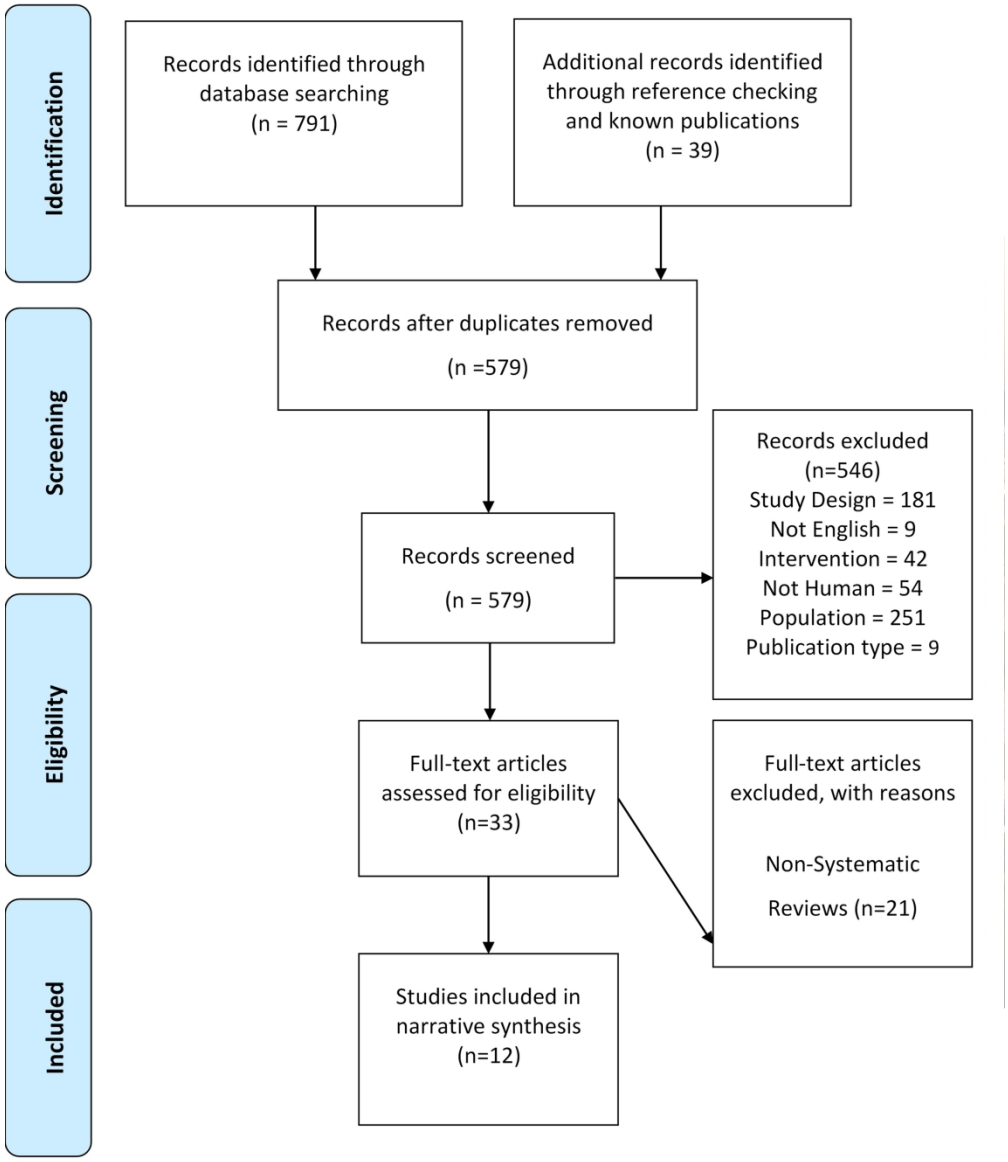
SUPPORTING INFORMATION CAPTIONS

Figure 1 PRISMA Flow diagram

Table 1 Review characteristics
Table 2 Primary studies included in each review and the number of included patients
Table 3 Risk of bias using ROBIS tool
Table 4 Results of individual reviews that report a meta-analysis for flail chest
Table 5 Results of individual reviews that report a narrative synthesis for flail chest
Table 6 Results of individual reviews that report a narrative synthesis for multiple rib fractures

S Appendix 1 Medline search strategy

S Appendix 2 Excluded studies



PRISMA Flow Diagram

262x313mm (300 x 300 DPI)

Additional file 1 MEDLINE search strategy (OVID interface)

1. (rib adj3 fracture*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

2. ((flail chest or stove? in) adj3 chest).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

3. (blunt chest adj3 trauma).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

4. extra thoracic injur*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

5. costal fracture*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

6. Flail Chest/

7. Rib Fractures/

8. 1 or 2 or 3 or 4 or 5 or 6 or 7

9. (fracture* adj3 fixation).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

10. bone screw*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

11. Bone plate*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

12. (suture adj3 fixation).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

13. judet strut.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

14. bioabsorbable plate*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

15. heavy suture*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

16. intramedullary splint*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

17. (metal adj2 fixation).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

18. ((plate* or strut) adj3 fixation*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

19. exp Internal Fixators/

20. fracture fixation/ or fracture fixation, internal/ or fracture fixation, intramedullary/

21. (fracture adj3 stabili?ation).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

22. 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21

23. 8 and 22

24. limit 23 to (humans and yr="1976 -Current")

Additional content 2 Excluded studies with reasons given for exclusion

1	Galan G, Penalver JC, Paris F, et al. BLUNT CHEST INJURIES IN 1696 PATIENTS. Eur J Cardiothorac Surg. 1992; 6: 284-7.	Study Design
2	Actis Dato GM, Aidala E and Ruffini E. Surgical management of flail chest. Ann Thorac Surg. 1999; 67: 1826-7.	Study Design
3	Ahmed Z and Mohyuddin Z. Management of flail chest injury: Internal fixation versus endotracheal intubation and ventilation. Journal of Thoracic and Cardiovascular Surgery. 1995; 110: 1676-80.	Study Design
4	Akkus M, Utkusavas A, Hanozu M, Kaya M and Bakir I. Stabilization of Flail Chest and Fractured Sternum by Minimally Invasive Repair of Pectus Excavatum. Thoracic and Cardiovascular Surgeon Reports. 2015; 4: 11-3.	Study Design
5	Althausen PL, Shannon S, Watts C, et al. Early surgical stabilization of flail chest with locked plate fixation. J Orthop Trauma. 2011; 25: 641-7.	Study Design
6	Ananiadou O, Karaiskos T, Givissis P and Drossos G. Operative stabilization of skeletal chest injuries secondary to cardiopulmonary resuscitation in a cardiac surgical patient. Interact Cardiovasc Thorac Surg. 2010; 10: 478-80.	Study Design
7	Attia RQ, Schulte KL and Whitaker DC. eReply: In patients with acute flail chest does surgical rib fixation improve outcomes in terms of morbidity and mortality? Interactive Cardiovascular and Thoracic Surgery. 2016; 23: 319-20.	Study Design
8	Bailey J, VanderHeiden T, Burlew CC, et al. Thoracic hyperextension injury with complete "bony disruption" of the thoracic cage: Case report of a potentially life-threatening injury. World Journal of Emergency Surgery. 2012; 7.	Study Design
9	Beelen R, Rumbaut J and De Geest R. Surgical stabilization of a rib fracture using an angle stable plate. Journal of Trauma - Injury, Infection and Critical Care. 2007; 63: 1159-60.	Study Design
10	Beltrami V, Martinelli G, Giansante P and Gentile K. An original technique for surgical stabilisation of traumatic flail chest. Thorax. 1978; 33: 528-9.	Study Design
11	Berthet JP, Solovei L, Tiffet O, et al. Chest-wall reconstruction in case of infection of the operative site: Is there any interest in titanium rib osteosynthesis. Eur J Cardiothorac Surg. 2013; 44: 866-74.	Study Design
12	Bibas BJ and Bibas RA. Operative stabilization of flail chest using a prosthetic mesh and methylmethacrylate. Eur J Cardiothorac Surg. 2006; 29: 1064-6.	Study Design
13	Bille A, Okiror L, Campbell A, Simons J and Routledge T. Evaluation of long-term results and quality of life in patients who underwent rib fixation with titanium devices after trauma. General Thoracic and Cardiovascular Surgery. 2013; 61: 345-9.	Study Design

14	Bille A, Okiror L, Karenovics W and Routledge T. Experience with titanium devices for rib fixation and coverage of chest wall defects. Interactive Cardiovascular and Thoracic Surgery. 2012; 15: 588-95.	Study Design
15	Bonne SL, Turnbull IR and Southard RE. Technique for repair of fractures and separations involving the cartilaginous portions of the anterior chest wall. Chest. 2015; 147: e199-e204.	Study Design
16	Borrelly J and Aazami MH. New insights into the pathophysiology of flail segment: The implications of anterior serratus muscle in parietal failure. Eur J Cardiothorac Surg. 2005; 28: 742-9.	Study Design
17	Bottlang M, Long WB, Phelan D, Fielder D and Madey SM. Surgical stabilization of flail chest injuries with MatrixRIB implants: A prospective observational study. Injury. 2013; 44: 232-8.	Study Design
18	Brotzu G, Montisci R, Pillai W and Sanna S. Chest injuries. A review of 195 patients. Ann Chir Gynaecol. 1988; 77: 155-9.	Study Design
19	Buyukkarabacak YB, Sengul AT, Celik B, et al. The Usefulness of Early Surgical Rib Stabilization in Flail Chest. Acta Chir Belg. 2015; 115: 408-13.	Study Design
20	Cacchione RN, Richardson JD and Seligson D. Painful nonunion of multiple rib fractures managed by operative stabilization. Journal of Trauma - Injury, Infection and Critical Care. 2000; 48: 319-21.	Study Design
21	Campbell N, Conaglen P, Martin K and Antippa P. Surgical stabilization of rib fractures using inion OTPS wraps-techniques and quality of life follow-up. Journal of Trauma - Injury, Infection and Critical Care. 2009; 67: 596-601.	Study Design
22	Caragounis EC, Olsen MF, Pazooki D and Granhed H. Surgical treatment of multiple rib fractures and flail chest in trauma: a one-year follow-up study. World Journal of Emergency Surgery. 2016; 11.	Study Design
23	Chapman BC, Herbert B, Rodil M, et al. RibScore: A novel radiographic score based on fracture pattern that predicts pneumonia, respiratory failure, and tracheostomy. J Trauma Acute Care Surg. 2016; 80: 95-101.	Study Design
24	Charafeddine AH, Stone ME, Reddy SH, Teperman SH, Kaban JM and Cohen-Levy WB. Anterior chest wall disassociation: A pattern associated with serious underlying injury. Am Surg. 2015; 81: E244-E5.	Study Design
25	Cho YH, Kim HK, Kang DY and Choi YH. Reoperative surgical stabilization of a painful nonunited rib fracture using bone grafting and a metal plate. J Orthop Trauma. 2009; 23: 605-6.	Study Design
26	De La Santa Barajas PM, Polo Otero MD, Delgado Sanchez- Gracian C, Leal Ruiloba S, Trinidad C and Choren Duran M. Surgical treatment for flail chest. Interactive Cardiovascular and Thoracic Surgery. 2012; 15: S5.	Study Design
27	De Moya M, Bramos T, Agarwal S, et al. Pain as an indication for rib fixation: A bi-institutional pilot study. Journal of Trauma -	Study Design

	Injury, Infection and Critical Care. 2011; 71: 1750-4.	
28	de Palma A, Sollitto F, Loizzi D, et al. Chest wall stabilization and reconstruction: Short and long-term results 5 years after the introduction of a new titanium plates system. Journal of Thoracic Disease. 2016; 8: 490-8.	Study Design
29	Dean NC, Van Boerum DH and Liou TG. Rib plating of acute and sub-acute non-union rib fractures in an adult with cystic fibrosis: a case report. BMC Res Notes. 2014; 7: 681.	Study Design
30	Defreest L, Tafen M, Bhakta A, et al. Open reduction and internal fixation of rib fractures in polytrauma patients with flail chest. Am J Surg. 2016; 211: 761-7.	Study Design
31	Dehghan N, de Mestral C, McKee MD, Schemitsch EH and Nathens A. Flail chest injuries: A review of outcomes and treatment practices from the National Trauma Data Bank. Journal of Trauma and Acute Care Surgery. 2014; 76: 462-8.	Study Design
32	Doben AR, Eriksson EA, Denlinger CE, et al. Surgical rib fixation for flail chest deformity improves liberation from mechanical ventilation. J Crit Care. 2014; 29: 139-43.	Study Design
33	Dunlop RLE, Tiong W, Veerasingam D and Kelly JL. Novel use of hand fracture fixation plates in the surgical stabilisation of flail chest. Journal of Plastic, Reconstructive and Aesthetic Surgery. 2010; 63: e51-e3.	Study Design
34	Engel C, Krieg JC, Madey SM, Long WB and Bottlang M. Operative chest wall fixation with osteosynthesis plates. Journal of Trauma - Injury, Infection and Critical Care. 2005; 58: 181-6.	Study Design
35	Evman S, Kolbas I, Dogruyol T and Tezel C. A Case of Traumatic Flail Chest Requiring Stabilization with Surgical Reconstruction. Thoracic and Cardiovascular Surgeon Reports. 2015; 4: 8-10.	Study Design
36	Fagevik Olsén M, Pazooki D and Granhed H. Recovery after stabilising surgery for 'flail chest'. Unfallchirurgie. 2013; 39: 501-6.	Study Design
37	Farquhar J, Almahrabi Y, Slobogean G, et al. No benefit to surgical fixation of flail chest injuries compared with modern comprehensive management: results of a retrospective cohort study. Canadian Journal of Surgery. 2016; 59: 299-303.	Study Design
38	Flagel BT, Luchette FA, Reed RL, et al. Half-a-dozen ribs: the breakpoint for mortality. Surgery. 2005; 138: 717-23; discussion 23-5.	Study Design
39	Gabram SGA, Devanney J, Jones D and Jacobs LM. Delayed hemorrhagic pericardial effusion: Case reports of a complication from severe blunt chest trauma. Journal of Trauma. 1992; 32: 794-800.	Study Design
40	Galvin IF, Costa R and Murton M. FRACTURED RIB WITH PENETRATING CARDIOPULMONARY INJURY. Ann Thorac Surg. 1993; 56: 558-9.	Study Design

41	Gardenbroek TJ, Bemelman M and Leenen LPH. Pseudarthrosis of the ribs treated with a locking compression plate: A report of three cases. Journal of Bone and Joint Surgery - Series A. 2009; 91: 1477-9.	Study Design
42	Gasparri MG, Almassi GH and Haasler GB. Surgical management of multiple rib fractures. Chest. 2003; 124: 295S-6S.	Study Design
43	George RJ and Stern HS. An approach to surgical fixation of traumatic costosternal diastasis. ANZ J Surg. 2014; 84: 594-5.	Study Design
44	Gerov I and Yablanski V. Damage control - Increasing the survival rates through emergency bone stabilization in a polytraumatized young patient. Injury. 2011; 42: S29.	Study Design
45	Ginsberg RJ and Kostin RF. 5. New approaches to the management of flail chest. Can Med Assoc J. 1977; 116: 613-5.	Study Design
46	Govaert G, Schuetz M and Peters P. Rib fixation for a traumatic 'stove-in chest': An option to consider. ANZ J Surg. 2012; 82: 276-7.	Study Design
47	Granetzny A, Abd El-Aal M, Emam E, Shalaby A and Boseila A. Surgical versus conservative treatment of flail chest. Evaluation of the pulmonary status. Interact Cardiovasc Thorac Surg. 2005; 4: 583-7.	Study Design
48	Granhed HP and Pazooki D. A feasibility study of 60 consecutive patients operated for unstable thoracic cage. J Trauma Manag Outcomes. 2014; 8: 20.	Study Design
49	Guernelli N, Bragaglia RB, Briccoli A, Mastrorilli M and Vecchi R. Technique for the management of anterior flail chest. Thorax. 1979; 34: 247-8.	Study Design
50	Gunn JM, Savola J and Isotalo K. Left-sided diaphragmatic and pericardial ruptures with subluxation of the heart after blunt trauma. Ann Thorac Surg. 2012; 93: 317-9.	Study Design
51	Haasler GB. Open fixation of flail chest after blunt trauma. Ann Thorac Surg. 1990; 49: 993-5.	Study Design
52	Hasenboehler EA, Bernard AC, Bottiggi AJ, et al. Treatment of traumatic flail chest with muscular sparing open reduction and internal fixation: Description of a surgical technique. Journal of Trauma - Injury, Infection and Critical Care. 2011; 71: 494-501.	Study Design
53	Hellberg K, de Vivie ER, Fuchs K, et al. Stabilization of flail chest by compression osteosynthesis--experimental and clinical results. Thorac Cardiovasc Surg. 1981; 29: 275-81.	Study Design
54	Igai H, Kamiyoshihara M, Nagashima T and Ohtaki Y. Rib fixation for severe chest deformity due to multiple rib fractures. Annals of Thoracic and Cardiovascular Surgery. 2012; 18: 458-61.	Study Design
55	Ivancic A, Saftic I, Cicvaric T, et al. Initial experience with external thoracic stabilization by the "figure of eight" osteosynthesis in	Study Design

	polytraumatized patients with flail chest injury. Coll Antropol. 2009; 33: 51-6.	
56	Jayle CP, Allain G, Ingrand P, et al. Flail chest in polytraumatized patients: surgical fixation using Stracos reduces ventilator time and hospital stay. Biomed Res Int. 2015; 2015: 624723.	Study Design
57	Kamiyoshihara M, Nagashima T, Ibe T and Takeyoshi I. Rupture of the diaphragm and pericardium with cardiac herniation after blunt chest trauma. General Thoracic and Cardiovascular Surgery. 2010; 58: 291-4.	Study Design
58	Kaplan T, Gulbahar G, Gundogdu AG and Han S. An unexpected complication of titanium rib clips. Ann Thorac Surg. 2014; 98: 2206-9.	Study Design
59	Ke S, Duan H, Cai Y, Kang J and Feng Z. Thoracoscopy-assisted minimally invasive surgical stabilization of the anterolateral flail chest using Nuss bars. Ann Thorac Surg. 2014; 97: 2179-82.	Study Design
60	Khandelwal G, Mathur RK, Shukla S and Maheshwari A. A prospective single center study to assess the impact of surgical stabilization in patients with rib fracture. Int J Surg. 2011; 9: 478-81.	Study Design
61	Kilic D, Findikcioglu A, Akin S, et al. Factors affecting morbidity and mortality in flail chest: Comparison of anterior and lateral location. Thoracic and Cardiovascular Surgeon. 2011; 59: 45-8.	Study Design
62	Kim JJ, Kim YH, Moon SW, Choi SY and Jeong SC. Nuss procedure for severe flail chest after blunt trauma. Ann Thorac Surg. 2015; 99: e25-7.	Study Design
63	Konstantinov IE, Saxena P and Wood DJ. Stabilisation of chronic flail chest: A novel approach of surgical fixation and osteogenesis. Thorax. 2009; 64: 265-6.	Study Design
64	Kruger M, Zinne N, Zhang RY, et al. Multidirectional Thoracic Wall Stabilization: A New Device on the Scene. Ann Thorac Surg. 2013; 96: 1846-9.	Study Design
65	Kulaylat AN, Chesnut CH, 3rd, Santos AP and Armen SB. Successful operative rib fixation of traumatic flail chest in a patient with osteogenesis imperfecta. Interact Cardiovasc Thorac Surg. 2014; 19: 518-9.	Study Design
66	Landreneau RJ, Hinson Jr JM, Hazelrigg SR, Johnson JA, Boley TM and Curtis JJ. Strut fixation of an extensive flail chest. Ann Thorac Surg. 1991; 51: 473-5.	Study Design
67	Lang M, Krumrey MT, Roder J, Ulmer J, Friederichs J and Buhren V. Late complications following blunt abdominal and thoracic trauma: Two case reports of a minimally invasive therapy. [German, English]. Chirurg. 2012; 83: 1078-81.	Study Design
68	Lang-Lazdunski L, Bonnet PM, Pons F, Brinquin L and Jancovici R. Traumatic extrathoracic lung herniation. Ann Thorac Surg.	Study Design

	2002; 74: 927-9.	
69	Lanier ST, Wetterau M, Smith-Singares E, et al. Management of pulmonary hernia through a flail segment in closed thoracic trauma using open reduction, internal fixation and pectoralis major flap reconstruction: A case report. Canadian Journal of Plastic Surgery. 2011; 19: 145-7.	Study Design
70	Lardinois D, Krueger T, Dusmet M, Ghisletta N, Gugger M and Ris HB. Pulmonary function testing after operative stabilisation of the chest wall for flail chest. Eur J Cardiothorac Surg. 2001; 20: 496-501.	Study Design
71	Lee SA, Hwang JJ, Chee HK, Kim YH and Lee WS. Flail chest stabilization with Nuss operation in presence of multiple myeloma. Journal of Thoracic Disease. 2014; 6: E43-E7.	Study Design
72	Lee SK and Kang DK. Nuss procedure for surgical stabilization of flail chest with horizontal sternal body fracture and multiple bilateral rib fractures. Journal of Thoracic Disease. 2016; 8: E390-E2.	Study Design
73	Lee SY, Lee SJ, Lee CS and Lee KR. Spontaneous fractures of judet struts. Journal of Trauma - Injury, Infection and Critical Care. 2009; 67: 214.	Study Design
74	Leenstra BS, Stolwijk A and Poeze M. Surgical stabilisation in a 13-year-old boy with traumatic flail chest. BMJ Case Rep. 2015; 2015 (no pagination).	Study Design
75	Majercik S, Cannon Q, Granger SR, Van Boerum DH and White TW. Regarding: Long-term patient outcomes after surgical stabilization of rib fractures. Am J Surg. 2015; 210: 199-200.	Study Design
76	Majercik S, Cannon Q, Granger SR, Vanboerum DH and White TW. Long-term patient outcomes after surgical stabilization of rib fractures. Am J Surg. 2014; 208: 88-92.	Study Design
77	Majercik S, Vijayakumar S, Olsen G, et al. Surgical stabilization of severe rib fractures decreases incidence of retained hemothorax and empyema. Am J Surg. 2015; 210: 1112-7.	Study Design
78	Marasco S, Cooper J, Pick A and Kossmann T. Pilot study of operative fixation of fractured ribs in patients with flail chest. ANZ J Surg. 2009; 79: 804-8.	Study Design
79	Marasco S, Liew S, Edwards E, Varma D and Summerhayes R. Analysis of bone healing in flail chest injury: Do we need to fix both fractures per rib? Journal of Trauma and Acute Care Surgery. 2014; 77: 452-8.	Study Design
80	Marasco S, Quayle M, Summerhayes R, Sutalo ID and Liovic P. An assessment of outcomes with intramedullary fixation of fractured ribs. J Cardiothorac Surg. 2016; 11.	Study Design

81	Marasco SF, Davies AR, Cooper J, et al. Prospective randomized controlled trial of operative rib fixation in traumatic flail chest. J Am Coll Surg. 2013; 216: 924-32.	Study Design
82	Maury JM, Roquet G, Marcotte G and David JS. Surgical fixation of rib fractures in chest wall trauma. Intensive Care Med. 2015; 41: 1483-4.	Study Design
83	Maxwell CA, Mion LC and Dietrich MS. Hospitalized injured older adults: clinical utility of a rib fracture scoring system. J Trauma Nurs. 2012; 19: 168-74; quiz 75-6.	Study Design
84	Mayberry JC, Ham LB, Schipper PH, Ellis TJ and Mullins RJ. Surveyed opinion of American trauma, orthopedic, and thoracic surgeons on rib and sternal fracture repair. J Trauma. 2009; 66: 875-9.	Study Design
85	Mayberry JC, Kroeker AD, Ham LB, Mullins RJ and Trunkey DD. Long-Term Morbidity, Pain, and Disability after Repair of Severe Chest Wall Injuries. Am Surg. 2009; 75: 389-94.	Study Design
86	Mayberry JC, Terhes JT, Ellis TJ, Wanek S and Mullins RJ. Absorbable Plates for Rib Fracture Repair: Preliminary Experience. Journal of Trauma - Injury, Infection and Critical Care. 2003; 55: 835-9.	Study Design
87	Menard A, Testart J, Philippe JM and Grise P. TREATMENT OF FLAIL CHEST WITH JUDET STRUTS. Journal of Thoracic and Cardiovascular Surgery. 1983; 86: 300-5.	Study Design
88	Messing JA, Gall V and Sarani B. Successful management of severe flail chest via early operative intervention. J Trauma Nurs. 2014; 21: 83-5.	Study Design
89	Metin B and Intepe YS. Operative ease and efficiency of nitinol memory rib plaque on the multiple costa and sternum fractures: Three-year clinical experience. International Journal of Clinical and Experimental Medicine. 2016; 9: 11510-7.	Study Design
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91	Michelitsch C, Acklin YP, Hassig G, Sommer C and Furrer M. Operative stabilisation of chest wall trauma: Single center report of initial management and longterm outcome. Respiration. 2016; 91 (5): 456.	Study Design
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565	Simon B, Ebert J, Bokhari F, et al. Management of pulmonary contusion and flail chest: An Eastern Association for the Surgery of Trauma practice management guideline. Journal of Trauma and Acute Care Surgery. 2012; 73: S351-S61.	Literature Review
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PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	3
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	3
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	4
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4-5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	S1
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	5-6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	6
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	5
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	6

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	6
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	N/A
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	7
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	8-13
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	16-17
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	17-18, 24-25, 27
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	17-33
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	14-16
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	N/A
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	33-34
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	36
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	37
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	37

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